

# REFERENCE NO.

# 22

In re application of: Hong Liu et al.  
Application No.: not yet assigned  
Filing Date: March 23, 2004  
Attorney Docket No.: 021288-002710US





PCT

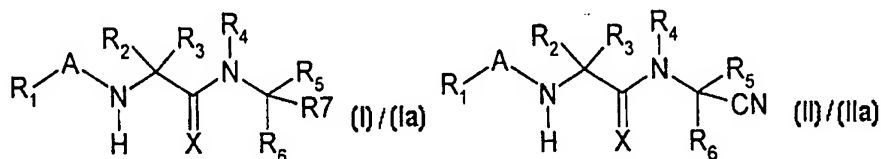
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : C07D 277/64, 263/32, 413/04, 295/20, C07C 311/42, A61P 9/10, 25/28, 37/02		A1	(11) International Publication Number: WO 00/51998
			(43) International Publication Date: 8 September 2000 (08.09.00)
(21) International Application Number: PCT/US99/26278		(81) Designated States: CA, JP, MX, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).	
(22) International Filing Date: 5 November 1999 (05.11.99)			
(30) Priority Data: 60/122,570 2 March 1999 (02.03.99) US		Published With international search report.	
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(54) Title: COMPOUNDS USEFUL AS REVERSIBLE INHIBITORS OF CATHEPSIN S



(57) Abstract

Disclosed are novel cathepsin S reversible inhibitory compounds of formulas (I),(Ia) and (II),(IIa) as defined herein. The compounds are useful for treating autoimmune diseases. Also disclosed are processes for making such novel compounds.

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## COMPOUNDS USEFUL AS REVERSIBLE INHIBITORS OF CATHEPSIN S

### RELATED APPLICATIONS

The benefit of prior provisional application Serial Number 60/122,570, filed on March 2,  
5 1999, is hereby claimed.

### TECHNICAL FIELD OF THE INVENTION

This invention relates to peptidyl cysteine protease inhibitors. The compounds are  
10 reversible inhibitors of the cysteine protease cathepsin S and are therefore useful in the  
treatment of autoimmune diseases. The invention also relates to processes for preparing  
such compounds and pharmaceutical compositions comprising them.

### BACKGROUND OF THE INVENTION

15 Cathepsin S is a member of the papain family, within the papain superfamily of cysteine  
proteases. The papain family is the largest group of cysteine proteases and includes  
proteases such as cathepsins B, H, K, L, O and S. (A.J. Barrett et al., 1996, Perspectives  
in Drug Discovery and Design, 6, 1). The cysteine proteases have important roles in  
20 human biology and diseases including atherosclerosis, emphysema, osteoporosis, chronic  
inflammation and immune disorders (H.A. Chapman et al., 1997, Ann. Rev. Physiol., 59,  
63). Cathepsin S plays a key role in regulating antigen presentation and immunity (H.A.  
Chapman, 1998, Current Opinion in Immunology, 10, 93; R. J. Riese et al., 1998, J. Clin.  
Invest., 101, 2351; R.J. Riese et al., 1996, Immunity, 4, 357).

25 The specificity of the immune response relies on processing of foreign protein and  
presentation of antigenic peptide at the cell surface. Antigenic peptide is presented bound  
to MHC Class II, a heterodimeric glycoprotein expressed in certain antigen presenting  
cells of hematopoietic lineage, such as B cells, macrophages and dendritic cells.  
30 Presentation of antigen to effector cells, such as T-cells, is a fundamental step in  
recognition of non-self and thus initiation of the immune response.

Recently MHC Class II heterodimers were shown to associate intracellularly with a third molecule designated invariant chain. Invariant chain facilitates Class II transport to the endosomal compartment and stabilizes the Class II protein prior to loading with antigen.

5 Invariant chain interacts directly with Class II dimers in the antigen-binding groove and therefore must be proteolyzed and removed or antigen cannot be loaded or presented. Current research suggests that invariant chain is selectively proteolyzed by cathepsin S, which is compartmentalized with MHC Class II complexes within the cell. Cathepsin S degrades invariant chain to a small peptide, termed CLIP, which occupies the antigen –

10 binding groove. CLIP is released from MHC Class II the interaction MHC Class II with HLA-DM, a MHC-like molecule thus freeing MHC Class II to associate with antigenic peptides. MHC Class II-antigen complexes are then transported to the cell surface for presentation to T-cells, and initiation of the immune response.

Cathepsin S, through proteolytic degradation of invariant chain to CLIP, provides a

15 fundamental step in generation of an immune response. It follows that inhibition of antigen presentation via prevention of invariant chain degradation by cathepsin S could provide a mechanism for immuno-regulation. Control of antigen-specific immune responses has long been desirable as a useful and safe therapy for autoimmune diseases. Such diseases include Crohn's disease and arthritis, as well as other T-cell-mediated

20 immune responses (C. Janeway and P. Travers, 1996, Immunobiology, The Immune System in Health and Disease, Chapter 12). Furthermore, cathepsin S, which has broad pH specificity, has been implicated in a variety of other diseases involving extracellular proteolysis, such as Alzheimer's disease (U. Muller-Ladner et al., 1996, Perspectives in Drug Discovery and Design, 6, 87) and atherosclerosis (G.K. Sukhova et al., 1998, J.

25 Clin. Invest., 102, 576).

Cysteine proteases are characterized by having a cysteine residue at the active site which serves as a nucleophile. The active site also contains a histidine residue. The imidazole ring on the histidine serves as a base to generate a thiolate anion on the active site

30 cysteine, increasing its nucleophilicity. When a substrate is recognized by the protease, the amide bond to be cleaved is directed to the active site, where the thiolate attacks the

carbonyl carbon forming an acyl-enzyme intermediate and cleaving the amide, liberating an amine. Subsequently, water cleaves the acyl-enzyme species regenerating the enzyme and liberating the other cleavage product of the substrate, a carboxylic acid.

- 5 A proposed mechanism of action of the cysteine protease inhibitors of this invention is that the inhibitors contain a functionality that can react (reversibly or irreversibly) with the active site cysteine. The reactive functionality is attached to a peptide or peptide mimic that can be recognized and accommodated by the region of the protease surrounding the active site. The nature of both the reactive functionality and the
- 10 remaining portion of the inhibitor determine the degree of selectivity and potency toward a particular protease.

Examples of reactive functionalities that have been described (D. Rasnick, 1996, Perspectives in Drug Discovery and Design, 6, 47) on cysteine protease inhibitors include

15 peptidyl diazomethanes, epoxides, monofluoroalkanes and acyloxymethanes, which irreversibly alkylate the cysteine thiol. Other irreversible inhibitors include Michael acceptors such as peptidyl vinyl esters and other carboxylic acid derivatives (S. Liu et al., J. Med Chem., 1992, 35, 1067) and vinyl sulfones (J.T. Palmer et al., 1995, J. Med Chem., 38, 3193).

20 Reactive functionalities that form reversible complexes with the active site cysteine include peptidyl aldehydes (R.P. Hanzlik et al., 1991, Biochim. Biophys. Acta., 1073, 33), which are non-selective, inhibiting both cysteine and serine proteases as well as other nucleophiles. Peptidyl nitriles (R.P. Hanzlik et al., 1990, Biochim. Biophys. Acta., 1035,

25 62) are less reactive than aldehydes and therefore more selective for the more nucleophilic cysteine proteases. Various reactive ketones have also been reported to be reversible inhibitors of cysteine proteases (D. Rasnick, 1996, *ibid*). In addition to reacting with the nucleophilic cysteine of the active site, reactive ketones may react with water, forming a hemiketal which may act as a transition state inhibitor.

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Examples of cathepsin S inhibitors have been reported previously. J.T. Palmer (U.S 5,776,718, 1998) described reversible peptidyl sulfones as inhibitors of cysteine proteases including cathepsin S. J.L. Klaus et al. (WO 9640737, 1996) described reversible inhibitors of cysteine proteases including cathepsin S, containing an ethylene diamine.

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Additional peptidyl nitriles or peptidyl ketoheterocycles have been reported either as protease inhibitors or as having other utilities. For example, both nitriles and ketoheterocycles are described by B.A. Rowe et al. (US 5714471, 1998) as protease inhibitors useful in the treatment of neurodegenerative diseases. Peptidyl nitriles are reported by B. Malcolm et al. (WO 9222570, 1992) as inhibitors of picornavirus protease. H. Saika et al. (WO 9512611, 1995) report peptidyl nitriles among compounds having endothelin receptor antagonist activity. B.J. Gour-Salin (Can. J. Chem., 1991, 69, 1288) and T.C. Liang (Arch. Biochim. Biophys., 1987, 252, 626) described peptidyl nitriles as inhibitors of papain. D.W. Woolley et al. (J. Org. Chem., 1963, 28, 2012) described a peptidyl nitrile as a chemical intermediate.

Peptidyl ketoheterocycles having protease inhibiting or other activities have been reported, include inhibitors of serine proteases described by R. D. Tung et al. (WO 9817679, 1998). Inhibitors of Factor X<sub>a</sub> have been described by C.K. Marlowe et al. (WO 9640744, 1996). Peptidyl ketoheterocycles useful in the treatment of thrombin related diseases have been described by M. Costanzo et al. (WO 9640742, 1996).

A reversible inhibitor presents a more attractive therapy than irreversible inhibitors. Even compounds with high specificity for a particular protease can bind non-target enzymes. An irreversible compound could therefore permanently inactivate a non-target enzyme, increasing the likelihood of toxicity. Furthermore, any toxic effects resulting from inactivation of the target enzyme would be mitigated by reversible inhibitors, and could be easily remedied by modified or lower dosing. Finally, covalent modification of an enzyme by an irreversible inhibitor could potentially generate an antibody response by acting as a hapten.

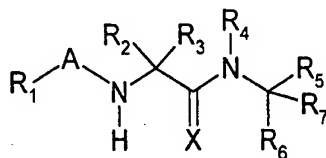
In light of the above, there is a clear need for compounds which reversibly and selectively inhibit cathepsin S, such inhibitors would be useful in therapy for antigen-specific immune responses as well as for indications in which cathepsin S exacerbates disease through extracellular activity.

### BRIEF DESCRIPTION OF THE INVENTION

The work cited above supports the principle that inhibition of cathepsin S and subsequent inhibition of antigen presentation will be beneficial in the treatment of various disease states. It is therefore an object of this invention to provide novel compounds that inhibit antigen presentation by virtue of reversible inhibition of the cysteine protease cathepsin S. It is a further object of the invention to provide methods for treating diseases and pathological conditions involving immune disorders such as rheumatoid arthritis. It is yet a further object of the invention to provide processes for preparation of the above-mentioned novel compounds.

### DETAILED DESCRIPTION OF THE INVENTION

The invention provides novel compounds of the formula (I):



(I)

A is -C(Y)- or -SO<sub>2</sub>-

Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

R<sub>1</sub> is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

5 R<sub>b</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a  
10 sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by  
15 alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

20 R<sub>c</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycle, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R<sub>2</sub> is H or alkyl;

R<sub>3</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>3</sub> is optionally substituted by one or more groups of the formula R<sub>d</sub>;

30 R<sub>d</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a  
35 sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by  
40 alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>c</sub>;



R<sub>c</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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R<sub>4</sub> is H or alkyl;

R<sub>5</sub> is H, alkyl or cycloalkyl;

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R<sub>6</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>6</sub> is optionally substituted by one or more groups of the formula R<sub>f</sub>;

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R<sub>f</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, heteroarylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

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R<sub>g</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by halogen, C1-5alkyl or C1-5alkoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

or R<sub>5</sub> together with R<sub>6</sub> form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

5 R<sub>h</sub> is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxy, carbonyl, arylalkoxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl or heteroaryl; halogen, hydroxy, carboxy and cyano;

10 R<sub>7</sub> is R<sub>8</sub>-C(Z)-;

wherein Z is O, S, or NR<sub>i</sub> wherein R<sub>i</sub> is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy and hydroxy;

15 R<sub>8</sub> is a 5-8 membered monocyclic heteroaryl or 8-11 membered bicyclic heteroaryl ring system, each of the monocyclic or bicyclic ring systems having 1-4 of the same or different heteroatoms selected from the group consisting of N, O and S wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

20 R<sub>j</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, alkoxycarbonyl, aryloxy, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxycarbonylamino, aryloxy, alkanoylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

35 R<sub>k</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy, alkanoylamino, arylalkoxy, arylalkoxy, arylalkoxy, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein

the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

- 5 X is O, S or N-OH;  
and the pharmacutrically acceptable derivatives thereof;

with the proviso that when R<sub>6</sub> is alkyl the alkyl must be substituted with R<sub>f</sub> wherein R<sub>f</sub> is not hydroxy, sulfhydryl or halogen.

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Preferred compounds of the formula (I) are those wherein:

R<sub>a</sub> is selected from the group consisting of H, alkyl and aryl;

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R<sub>1</sub> is C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranal, thiopyranal, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

25

R<sub>b</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be

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R<sub>c</sub> is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

40 R<sub>d</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothieryl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, 45 isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxy-carbonyl,

35 R<sub>c</sub> is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

40 R<sub>6</sub> is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R<sub>6</sub> is optionally substituted by one or more R<sub>6</sub>

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morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from  
 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
 isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,  
 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,  
 5 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl,  
 isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and  
 phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8  
 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl  
 wherein the nitrogen atom may be independently mono or di-substituted by C1-8  
 10 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,  
 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl,  
 15 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,  
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl  
 and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the  
 sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur  
 atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the  
 20 sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either  
 nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl  
 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,  
 thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group  
 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl,  
 25 isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl,  
 pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,  
 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
 alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy,  
 30 arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl,  
 arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono  
 or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of  
 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl  
 or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 35 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,  
 tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,  
 isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
 benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl,  
 carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy,  
 40 cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by  
 one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl,  
 aryl optionally substituted by halogen, C1-3alkyl or C1-3alkoxy;  
 45 heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;

heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl and arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5  $R_h$  is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy carbonyl, aryloxy carbonyl, arylC1-8alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group  
 10 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, carboxy and cyano;

15  $R_8$  is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, triazolyl, tetrazolyl, purinyl, quinoliziny, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl,  
 20 quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

25  $R_j$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,  
 30 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of  
 35 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by  
 40 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl



selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,

imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,  
thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,  
isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,  
5 quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
alkoxycarbonylamino, aryloxycarbonylamino, arylalkoxycarbonylamino,  
arylalkoxycarbonylaminoalkyl, C1-8 alkylcarbamoyloxy,  
arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,  
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom  
10 may be independently mono or di-substituted by alkyl, aryl, heterocyclyl  
selected from the group consisting of pyrrolidinyl, piperidinyl,  
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl  
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,  
15 tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,  
indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,  
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;  
20 X is O or S.

More preferred compounds of the formula (I) are those wherein:

25 Y is O or S;

R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group  
30 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranlyl,  
thiopyranlyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of  
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,  
pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or  
35 amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,  
naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl  
40 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,  
quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy,  
C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
45 wherein the nitrogen atom may be independently mono or di-substituted by C1-8  
alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,

5 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,  
 10 quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino,  
 aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a  
 sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a  
 sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently  
 15 substituted by alkyl, aryl, heterocyclyl selected from the group consisting of  
 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl  
 or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,  
 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
 benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5  
 20 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be  
 independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from  
 the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,  
 25 piperazinyl and indolinyl or heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,  
 pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl,  
 quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro,  
 30 amidino and guanidino,  $R_b$  may be further optionally substituted by one or more  
 $R_c$ ;

30  $R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,  
 aryl, heterocyclyl selected from the group consisting of piperidinyl,  
 morpholinyl and piperazinyl; heteroaryl selected from the group consisting  
 of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and  
 pyridinyl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano,  
 nitro, amidino and guanidino;

35  $R_2$  is H or C1-3 alkyl;

$R_3$  is H, C1-5 alkyl, C3-7 cycloalkyl or aryl, wherein  $R_3$  is optionally substituted by one  
 or more  $R_d$ ;

40  $R_d$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from  
 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
 triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl,  
 45 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl,  
 isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5alkanoyl,

aroyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_4$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_4$  is H or C1-3 alkyl;

$R_5$  is H or C1-8 alkyl;

$R_6$  is H, C1-5 alkyl, C3-7 cycloalkyl or aryl wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

R<sub>f</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,

benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>h</sub> is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, carboxy and cyano;

R<sub>i</sub> is alkoxy, aryloxy or hydroxy;

5 R<sub>8</sub> is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliziny, quinoliny, isoquinoliny, cinnoliny, phthalazinyl, quinazoliny, quinoxaliny, naphthyridiny, pteridiny, carbazolyl, acridiny and phenazinyl, wherein  
10 any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

R<sub>j</sub> is selected from the group consisting of C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from  
15 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl; arylC1-8alkyl, C1-8alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl  
20 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either  
25 nitrogen atom may be independently substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy,, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group  
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consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

R<sub>k</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkoxycarbonylamino, aryloxycarbonylamino, arylC1-8alkoxycarbonylamino, arylalkoxycarbonylamino, C1-8alkyl, C1-8alkylcarbamoyloxy, arylcarbamoyloxy, C1-8alkylsulfonylamino, arylsulfonylamino, C1-8alkylaminosulfonyl, arylaminosulfonyl, amino



wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino.

Even more preferred compounds of the formula (I) are those wherein:

Y is O;

R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>6</sub>;

R<sub>6</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from

the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, and cyano;

$R_2$  is H or methyl;

$R_3$  is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

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R<sub>4</sub> is H or methyl;

10 R<sub>5</sub> is H or C1-5 alkyl;

R<sub>6</sub> is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl or naphthyl wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

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R<sub>f</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, 20 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl 25 wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, 30 quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 35 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, 40 C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of 45 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,

quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

5 R<sub>g</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; naphthyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, 10 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl 15 wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, 20 benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl 25 selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, C1-5 alkoxycarbonylamino, 30 aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, 35 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;

40 R<sub>h</sub> is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl

selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano;

Z is O or S;

10

R<sub>8</sub> is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliziny, quinolinyl, isoquinolinyl, cinnoliny, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more groups of the formula R<sub>j</sub>;

20

R<sub>j</sub> is selected from the group consisting of C1-5alkyl, C3-6cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, arylC1-5alkyl, C1-5alkoxy, aryloxy, arylC1-5alkoxy, C1-5alkoxycarbonyl, aryloxycarbonyl, C1-5alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkanoylamino, aroylamino, C1-5alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5alkylsulfonylamino, arylsulfonylamino, C1-5alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl,

45

thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

R<sub>k</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, tetrazolyl and pyridinyl, C1-3 alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, aryl, heterocyclyl selected from the group consisting of morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, and pyridinyl, C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl, phenyl, naphthyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-3alkoxycarbonylamino, aryloxycarbonylamino, arylC1-3alkoxycarbonylamino, benzyloxycarbonylamino, C1-5alkyl, C1-3alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro;

and

X is O.

Yet even more preferred compounds of the formula (I) are those wherein:

R<sub>1</sub> is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,

imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

5  $R_b$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, 10 benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, 15 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl or naphthyl; C1-5 20 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl 25 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

30  $R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

$R_2$  is H;

35  $R_3$  is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

40  $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, 45 aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl,

5 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of  
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,  
C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be  
oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be  
10 oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group  
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl  
and indolyl, C1-5 alkoxy-carbonylamino, C1-5 alkylcarbamoxyloxy,  
arylcabamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein  
15 the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl,  
phenyl, heterocyclyl selected from the group consisting of piperidinyl,  
morpholinyl and piperazinyl or heteroaryl selected from the group consisting of  
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,  
halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally  
substituted by one or more  $R_e$ ;

20  $R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl,  
phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy,  
aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

wherein the configuration at the stereocenter defined by  $R_2$  and  $R_3$  and the carbon they  
are attached to is L;

25  $R_4$  is H;

30  $R_5$  is H or C1-3 alkyl;

$R_6$  is H, C1-5 alkyl, C3-6 cycloalkyl or phenyl. wherein  $R_6$  is optionally substituted by  
one or more  $R_f$ ;

35  $R_f$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl,  
naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group  
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl,  
indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,  
40 quinoliny and isoquinoliny, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, pyridylC1-  
5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxy-carbonyl,  
aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen  
atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or  
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
45 oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino,  
aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a



5 sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a  
 sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized  
 to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
 independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxy-carbonylamino,  
 C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom  
 10 may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl,  
 heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and  
 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy,  
 15 oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more  
 R<sub>g</sub>;

20 R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl,  
 phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl  
 25 selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl and piperazinyl; heteroaryl selected from the group  
 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
 pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy,  
 arylC1-3alkoxy, C1-5 alkoxy-carbonyl, aryloxy-carbonyl, C1-5  
 30 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be  
 independently mono or di-substituted by C1-5 alkyl or aryl; C1-5  
 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may  
 be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may  
 be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom  
 35 may be independently substituted by C1-5 alkyl or aryl; C1-5  
 alkoxy-carbonylamino, aryloxy-carbonylamino, C1-5 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom  
 40 may be independently mono or di-substituted by C1-5 alkyl or aryl;  
 halogen, hydroxy, oxo, carboxy and cyano;

35 R<sub>h</sub> is selected from the group consisting of C1-5 alkyl, phenyl, C1-5  
 alkoxy-carbonyl, aryloxy-carbonyl, arylC1-3alkoxy-carbonyl, carbamoyl wherein  
 the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-  
 6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, halogen, hydroxy, carboxy and  
 cyano;

40 wherein Z is O;

45 R<sub>8</sub> is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl,  
 imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,

benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

R<sub>j</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, arylC1-3alkyl, C1-3alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, morpholinyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; C1-3 alkoxycarbonylamino, aryloxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; halogen, hydroxy, oxo, carboxy, cyano and nitro, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

R<sub>k</sub> is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, morpholinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; arylC1-3alkoxycarbonylamino, benzyloxycarbonylamino, C1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, naphthyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro.

Still yet even more preferred compounds of the formula (I) are those wherein:

5  $R_1$  is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

10  $R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3  
15 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl; C1-5 alkanoylamino, aroylamino, C1-3  
20 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl,  
25 heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

30

$R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

35  $R_3$  is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl,  
40 imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently  
45 substituted by C1-3 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be

independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

5 R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

10 R<sub>f</sub> is H, C1-5 alkyl or phenyl wherein R<sub>f</sub> is optionally substituted by one or more R<sub>g</sub>;

R<sub>f</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridyl, C1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3  
15 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen  
20 atom may be independently substituted by C1-5 alkyl or phenyl; C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

25 R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5  
30 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5  
35 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

40

R<sub>h</sub> is selected from the group consisting of C1-3 alkyl, phenyl, C1-3  
45 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, phenyl, benzyl, halogen, hydroxy, carboxy and cyano;

5  $R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

10  $R_j$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, benzyl, C1-3alkoxy, phenoxy, benzyloxy, C1-3alkoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, thiazolyl, imidazolyl or pyridinyl; C1-3 alkoxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; halogen, hydroxy, carboxy, cyano and nitro,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

25  $R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, pyridinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl and thiazolyl, benzyloxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl, halogen, hydroxy, carboxy, cyano and nitro.

40 Even much more preferred compounds of the formula (I) are those wherein:

45  $R_1$  is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyranyl, thiopyranyl or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

5  $R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-  
10 substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl,, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

15  $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3alkoxy, C1-5alkoxycarbonyl, C1-5alkanoyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-  
20 3alkyl or phenyl; C1-5alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3alkoxycarbonylamino, C1-3alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

25  $R_e$  is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

30  $R_5$  is H or methyl;

$R_6$  is C1-5 alkyl or phenyl, wherein  $R_6$  is optionally substituted by one or more groups of the formula  $R_f$ ,

35  $R_f$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom  
40 may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

45  $R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen or methyl; C1-3 alkoxy, aryloxy, benzyloxy, C1-3

alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

$R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, benzyloxy and carboxy;

$R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzimidazolyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_i$ ;

$R_j$  is selected from the group consisting of methyl, cyclohexyl, phenyl, furanyl, thienyl, benzyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; acetylamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, C1-3 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy and cyano,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of methyl, phenyl, furanyl, thienyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetylamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylamino C1-3alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy, cyano and nitro.

Yet even more preferred compounds of the formula (I) are those wherein:

A is -C(O)- or -SO<sub>2</sub>-;

$R_1$  is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy;

$R_3$  is C1-5 alkyl or C5-6 cycloalkyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

$R_f$  is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of methyl, phenyl optionally substituted by halogen or methyl; methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy and carboxy;



R<sub>8</sub> is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

5 R<sub>j</sub> is selected from the group consisting of methyl, phenyl, furanyl, thienyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetylamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, amino  
10 wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; halogen, hydroxy, carboxy and cyano, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

15 R<sub>k</sub> is selected from the group consisting of methyl, phenyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or  
20 di-substituted by C1-3alkyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy, cyano and nitro.

25 Penultimately preferred compounds of the formula (I) are those wherein:

R<sub>1</sub> is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

30 R<sub>b</sub> is selected from the group consisting of, pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy and carboxy, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

35 R<sub>c</sub> is selected from the group consisting of methoxy, halogen and hydroxy;

40 R<sub>d</sub> is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

45 R<sub>e</sub> is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

R<sub>5</sub> is H;

5 R<sub>f</sub> is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

10 R<sub>g</sub> is selected from the group consisting of methyl, phenyl optionally substituted by halogen; methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

15 R<sub>8</sub> is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

20 R<sub>j</sub> is selected from the group consisting of methyl, phenyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; methoxycarbonylamino, halogen, hydroxy and carboxy, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

25 R<sub>k</sub> is selected from the group consisting of methyl, phenyl, methoxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; benzyloxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; halogen, hydroxy and carboxy.

30

35 Ultimately preferred compounds of the formula(I) are those wherein:

R<sub>1</sub> is phenyl or 4-morpholinyl, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

40 R<sub>b</sub> is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino, R<sub>b</sub> may be further optionally substituted by a halogen atom;

R<sub>3</sub> is C1-5 alkyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

45 R<sub>d</sub> is selected from the group consisting of C3-6 cycloalkyl and phenyl, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

$R_e$  is selected from the group consisting of methyl and halogen;

$R_f$  is C1-5 alkyl optionally substituted by one or more  $R_g$ ;

$R_f$  is selected from the group consisting of C5-6 cycloalkyl, phenyl, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, and halogen.  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

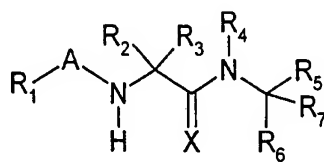
$R_g$  is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy;

$R_h$  is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_h$  can be optionally substituted by one or more  $R_i$ ;

$R_j$  is selected from the group consisting of phenyl, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or disubstituted by methyl or phenyl; methoxycarbonylamino and halogen,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of phenyl, methoxycarbonyl, carbamoyl, benzyloxycarbonylamino and halogen.

In another embodiment of the invention there are provided novel compounds of the formula (Ia):



(Ia)

wherein:

A is -C(Y)- or -SO<sub>2</sub>-

Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

R<sub>1</sub> is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

5 R<sub>b</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a  
10 sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by  
15 alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

20 R<sub>c</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycle, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R<sub>2</sub> is H or alkyl;

R<sub>3</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>3</sub> is optionally substituted by one or more groups of the formula R<sub>d</sub>;

30 R<sub>d</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to  
35 a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by  
40 alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5

R<sub>4</sub> is H or alkyl;

10

R<sub>5</sub> is H, alkyl or cycloalkyl;

R<sub>6</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>6</sub> is optionally substituted by one or more groups of the formula R<sub>f</sub>;

15

R<sub>f</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, heteroarylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

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R<sub>g</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by halogen, C1-5alkyl or C1-5alkoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

or R<sub>5</sub> together with R<sub>6</sub> form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

5 R<sub>h</sub> is selected from the group consisting of alkyl, aryl, alkoxy carbonyl, aryloxy carbonyl, arylalkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl or heteroaryl; halogen, hydroxy, carboxy and cyano;

$R_7$  is  $R_8-C(Z)-$ ;

wherein Z is O, S, or NR<sub>i</sub> wherein R<sub>i</sub> is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy and hydroxy;

15 R<sub>8</sub> is a 5-8 membered monocyclic heteroaryl or 8-11 membered bicyclic heteroaryl ring system, each of the monocyclic or bicyclic ring systems having 1-4 of the same or different heteroatoms selected from the group consisting of N, O and S wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>i</sub>;

20 R<sub>j</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; 25 alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

35 R<sub>k</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl,  
heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl,  
aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen  
40 atom may be independently mono or di-substituted by alkyl, aryl,  
heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein  
the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein  
the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein  
either nitrogen atom may be independently substituted by alkyl, aryl,  
heterocyclyl or heteroaryl, alkoxy carbonylamino, aryloxy carbonylamino,  
45 arylalkoxy carbonylamino, arylalkoxy carbonylaminoalkyl,  
alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino,  
arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein

the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein  $R_k$  may be further optionally substituted by  $R_i$ ;

5

$R_i$  is selected from the group consisting of alkyl, cycloalkyl, aryl, and benzyl;

X is O, S or N-OH;

10

and the pharmacutrically acceptable derivatives thereof;

with the following provisos:

15

when  $R_6$  is alkyl the alkyl must be substituted with  $R_f$  wherein  $R_f$  is not hydroxy, sulfhydryl or halogen;

and

when  $R_1$  is C1alkyl then  $R_b$  cannot be carbamoyl, alkanoylamino, aroylamino, ureido, alkoxy-carbonylamino, aryloxy-carbonylamino, alkylsulfonylamino, arylsulfonylamino, amino, amidino or guanidino wherein each said  $R_b$  is linked to said  $R_1$  via the nitrogen atom thereof.

20

25 Preferred compounds of the formula (Ia) are those wherein:

$R_a$  is selected from the group consisting of H, alkyl and aryl;

30  $R_1$  is C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

35

40  $R_b$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and

45

phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxy carbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy carbonylamino, aryloxy carbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;



R<sub>3</sub> is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>4</sub>;

5 R<sub>4</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>4</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>e</sub> is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>5</sub> is H or alkyl;

R<sub>6</sub> is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

R<sub>f</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,

oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ :

$R_g$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, C1-3alkyl or C1-3alkoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl or phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonfylamino, arylsulfonfylamino, alkylaminosulfonfyl and arylaminosulfonfyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,

piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_h$  is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy carbonyl, aryloxy carbonyl, arylC1-8alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, carboxy and cyano;

$R_g$  is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, tetrazolyl, purinyl, quinoliziny, quinolinyl, isoquinolinyl, cinnoliny, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above  $R_g$  can be optionally substituted by one or more  $R_j$ ;

$R_j$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl,

5 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, benzoxazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny,  
 quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino,  
 aroylamino, alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or  
 sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or  
 sulfone, arylalkylthio wherein the sulfur atom may be oxidised to a sulfoxide or  
 sulfone, ureido wherein either nitrogen atom may be independently substituted by  
 10 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,  
 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl,  
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,  
 15 quinoliny, isoquinoliny, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl  
 and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8  
 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,  
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be  
 independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from  
 20 the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,  
 piperazinyl and indolinyl; heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl,  
 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 25 benzthiazolyl, benzoxazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny,  
 quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy,  
 oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>j</sub> may be further optionally  
 substituted by one or more R<sub>k</sub>;

30 R<sub>k</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;  
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,  
 35 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, benzoxazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny,  
 quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl,  
 alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl,  
 40 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be  
 independantly mono or di-substituted by alkyl, aryl, heterocyclyl selected  
 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,  
 thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl,  
 45 isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,  
 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,

5 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,  
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl,  
 phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, alkylthio  
 wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio  
 wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido  
 wherein either nitrogen atom may be independently substituted by alkyl,  
 aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl,  
 10 heteroaryl selected from furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,  
 imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,  
 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,  
 isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
 benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,  
 quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
 15 alkoxycarbonylamino, aryloxy carbonylamino, arylalkoxy carbonylamino,  
 arylalkoxy carbonylaminoalkyl, C1-8 alkyl carbamoyloxy,  
 aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino,  
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom  
 may be independently mono or di-substituted by alkyl, aryl, heterocyclyl  
 20 selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,  
 piperazinyl and indolinyl, heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl,  
 isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,  
 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,  
 25 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,  
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl,  
 phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano,  
 nitro, amidino and guanidino, wherein  $R_k$  may be further optionally  
 substituted by  $R_i$ ;

30

$R_i$  is selected from the group consisting of C1-5 alkyl, C3-7  
 cycloalkyl, phenyl and benzyl;

35 and  
 X is O or S.

40 More preferred compounds of the formula (Ia) are those wherein:

Y is O or S;

45  $R_i$  is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group  
 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranlyl,

thiopyranyl, piperaziny and indoliny, heteroaryl selected from the group consisting of furanyl, thienyl, pyrroly, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridiny, pyrimidinyl, pyraziny, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinoliny, isoquinoliny, quinazoliny and quinoxaliny or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholiny, thiomorpholiny, piperaziny and indoliny, heteroaryl selected from the group consisting of furanyl, thienyl, pyrroly, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridiny, pyrimidinyl, pyraziny, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinoliny, isoquinoliny, quinazoliny and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholiny, thiomorpholiny, piperaziny and indoliny or heteroaryl selected from the group consisting of furanyl, thienyl, pyrroly, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridiny, pyrimidinyl, pyraziny, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinoliny, isoquinoliny, quinazoliny and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholiny, thiomorpholiny, piperaziny and indoliny or heteroaryl selected from the group consisting of furanyl, thienyl, pyrroly, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridiny, pyrimidinyl, pyraziny, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinoliny, isoquinoliny, quinazoliny and quinoxaliny, C1-5 alkoxycarbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholiny, thiomorpholiny, piperaziny and indoliny or heteroaryl selected from the group consisting of furanyl, thienyl, pyrroly, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridiny, pyrimidinyl, pyraziny, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinoliny, isoquinoliny, quinazoliny and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholiny and piperaziny; heteroaryl selected from the group consisting

of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5 R<sub>2</sub> is H or C1-3 alkyl;

R<sub>3</sub> is H, C1-5 alkyl, C3-7 cycloalkyl or aryl, wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

10 R<sub>d</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, 15 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkanoyl, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of 20 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and 25 quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, 30 piperazinyl and indolinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 35 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected 40 from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>d</sub> may be further optionally 45 substituted by one or more R<sub>e</sub>;



R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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R<sub>4</sub> is H or C1-3 alkyl;

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R<sub>5</sub> is H or C1-8 alkyl;

R<sub>6</sub> is H, C1-5 alkyl, C3-7 cycloalkyl or aryl wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

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R<sub>f</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,

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thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and

5  $R_h$  is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxy carbonyl, aryloxy carbonyl, arylC1-5alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group  
10 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and  
15 quinoxalinyl, halogen, hydroxy, carboxy and cyano;

20 R<sub>8</sub> is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizynyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolizynyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, 25 quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

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sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8 alkyl, aryl, heterocycl

5 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl,

10 benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxy carbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocycl

15 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

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R<sub>k</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocycl

30 selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxy carbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-substituted by C1-8alkyl, aryl, heterocycl

35 selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or

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sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or  
 sulfone, ureido wherein either nitrogen atom may be independently  
 substituted by C1-8alkyl, aryl, heterocyclyl selected from the group  
 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,  
 5 piperazinyl and indolinyl, heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl,  
 isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,  
 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,  
 10 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,  
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl,  
 phenothiazinyl and phenoxazinyl, C1-8alkoxycarbonylamino,  
 aryloxycarbonylamino, arylC1-8alkoxycarbonylamino,  
 arylalkoxycarbonylaminoC1-8alkyl, C1-8 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-8alkylsulfonylamino, arylsulfonylamino, C1-  
 15 8alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom  
 may be independently mono or di-subsituted by C1-8alkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;  
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 20 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,  
 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,  
 quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
 25 halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  
 wherein  $R_k$  may be further optionally substituted by  $R_i$ .

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Even more preferred compounds of the formula (Ia) are those wherein:

Y is O;

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$R_1$  is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group  
 consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and  
 thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino  
 40 wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

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$R_b$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,  
 naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, and cyano;

$R_2$  is H or methyl;

$R_3$  is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein

5 either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein  
 10 the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may  
 15 be further optionally substituted by one or more R<sub>e</sub>;

20 R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

25 R<sub>4</sub> is H or methyl;

30 R<sub>5</sub> is H or C1-5 alkyl;

35 R<sub>6</sub> is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl or naphthyl wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

40 R<sub>f</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5  
 45 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio

wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; naphthyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5



alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_h$  is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, arylC1-3alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano;

25 Z is O or S;

$R_8$  is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliziny, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxaliny, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above  $R_8$  can be optionally substituted by one or more groups of the formula  $R_j$ ;

$R_j$  is selected from the group consisting of C1-5alkyl, C3-6cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, arylC1-5alkyl, C1-5alkoxy, aryloxy, arylC1-5alkoxy, C1-5alkoxy carbonyl, aryloxy carbonyl, C1-5alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by C1-5alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from furanyl, thienyl, pyrrolyl,

oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkanoylamino, aroylamino, C1-5alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-5alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoxyloxy, arylcarbamoxyloxy, C1-5alkylsulfonylamino, arylsulfonylamino, C1-5alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

R<sub>k</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, C1-3 alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, aryl, heterocyclyl selected from the group consisting of morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, and pyridinyl, C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl, phenyl, naphthyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-3alkoxycarbonylamino, aryloxycarbonylamino, arylC1-3alkoxycarbonylamino, benzyloxycarbonylamino, C1-5alkyl, C1-3 alkylcarbamoxyloxy, arylcarbamoxyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the

group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, wherein  $R_k$  may be further optionally substituted by  $R_i$ ;

$R_i$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl and phenyl.

Yet even more preferred compounds of the formula (Ia) are those wherein:

$R_1$  is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl or naphthyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl,

halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

5  $R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

$R_2$  is H;

10  $R_3$  is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

15  $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, 20 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be 25 independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkoxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, 30 phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

35  $R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

40 wherein the configuration at the stereocenter defined by  $R_2$  and  $R_3$  and the carbon they are attached to is L;

45  $R_4$  is H;

R<sub>5</sub> is H or C1-3 alkyl;

- 5 R<sub>6</sub> is H, C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

10 R<sub>f</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothieryl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxycarbonyl, 15 aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be 20 independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more 25 R<sub>g</sub>;

30 R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 35 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl; C1-5 40 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5

alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; halogen, hydroxy, oxo, carboxy and cyano;

5

$R_h$  is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, halogen, hydroxy, carboxy and cyano;

10

wherein Z is O;

15

$R_g$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, wherein any of the above  $R_g$  can be optionally substituted by one or more  $R_j$ ;

20

$R_j$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, arylC1-3alkyl, C1-3alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by C1-3alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, morpholinyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-3 alkoxycarbonylamino, aryloxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbstituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,

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benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy, cyano and nitro,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyrimidinyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; arylC1-3alkoxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, methylcarbamoyloxy, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, wherein  $R_k$  may be further optionally substituted by  $R_i$ ;

$R_i$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl and phenyl.

Still yet even more preferred compounds of the formula (Ia) are those wherein:

$R_1$  is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl and benzthiazolyl; C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

$R_3$  is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_6$  is H, C1-5 alkyl or phenyl wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridyl, C1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur



atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-3 alkoxy-carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxy-carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxy-carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

$R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy-carbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, phenyl, benzyl, halogen, hydroxy, carboxy and cyano;

$R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

$R_j$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyrimidinyl, benzyl, C1-3alkoxy, phenoxy, benzyloxy, C1-3alkoxy-carbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, thiazolyl, imidazolyl and pyridinyl; C1-3 alkoxy-carbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-

3alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl; halogen, hydroxy, carboxy, cyano and nitro,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyridinyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by methyl, phenyl, furanyl, thienyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl and thiazolyl, benzyloxycarbonylamino, benzyloxycarbonylamino C1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-susbstituted by C1-3alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl, halogen, hydroxy, carboxy, cyano and nitro, wherein  $R_k$  may be further optionally substituted by  $R_l$ ;

$R_l$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl and phenyl.

Even much more preferred compounds of the formula (Ia) are those wherein:

$R_1$  is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyranyl, thiopyranyl or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

5  $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3alkoxy, C1-5alkoxycarbonyl, C1-5alkanoyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl; C1-5alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3alkoxycarbonylamino, C1-3alkylsulfonylamino, amino wherein the nitrogen atom may be independently  
10 mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

15  $R_e$  is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_5$  is H or methyl;

20  $R_6$  is C1-5 alkyl or phenyl, wherein  $R_6$  is optionally substituted by one or more groups of the formula  $R_f$ ,

25  $R_f$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further  
30 optionally substituted by one or more  $R_g$ ;

35  $R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen or methyl; C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

40  $R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, benzyloxy and carboxy;

$R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, benzimidazolyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

5  $R_j$  is selected from the group consisting of C1-5 alkyl, cyclohexyl, phenyl, piperidinyl, furanyl, thienyl, pyridinyl, benzyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by methyl, phenyl, furanyl, thienyl; acetyl amino, benzoyl amino, ureido wherein either nitrogen atom may be  
10 independently substituted by methyl or phenyl; methoxycarbonyl amino, C1-3 alkylsulfonyl amino, arylsulfonyl amino, amino wherein the nitrogen atom may be independently mono or di-susbtituted by methyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy and cyano,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

15  $R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, piperazinyl, furanyl, thienyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by  
20 methyl or phenyl; acetyl amino, benzoyl amino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonyl amino, benzyloxycarbonyl amino C1-5 alkyl, amino wherein the nitrogen atom may be independently mono or di-susbtituted by C1-3 alkyl, phenyl, furanyl, or thienyl; halogen, hydroxy, carboxy,  
25 cyano and nitro, wherein  $R_k$  may be further optionally substituted by  $R_l$ ;

$R_l$  is selected from the group consisting of methyl, C3-6 cycloalkyl and phenyl.

30

Yet even more preferred compounds of the formula (Ia) are those wherein:

35 A is  $-C(O)-$  or  $-SO_2-$ ;

$R_1$  is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

40

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-  
45 substituted by C1-3 alkyl or phenyl; C1-5 alkanoyl amino, aroyl amino, C1-5 alkylsulfonyl amino, arylsulfonyl amino, amino wherein the nitrogen atom may be

independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_5$  may be further optionally substituted by one or more  $R_c$ ;

5  $R_c$  is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy;

$R_3$  is C1-5 alkyl or C5-6 cycloalkyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

10  $R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

15  $R_e$  is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

20  $R_f$  is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

25  $R_g$  is selected from the group consisting of methyl, phenyl optionally substituted by halogen or methyl; methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy and carboxy;

30  $R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

35  $R_j$  is selected from the group consisting of C1-5 alkyl, phenyl, furanyl, thienyl, piperidinyl, pyridinyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by methyl or phenyl; acetylamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-susbtituted by methyl, phenyl; halogen, hydroxy, carboxy and cyano,  $R_j$  may be further optionally substituted by one or more  $R_k$ ; and

40  
45

5  $R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independantly mono or di-susstituted by methyl or phenyl; ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-susstituted by C1-3alkyl, phenyl, furanyl and thienyl; halogen, hydroxy, carboxy, cyano and nitro, wherein  $R_k$  may be further optionally substituted by  $R_i$ ;

10  $R_i$  is selected from the group consisting of methyl and phenyl.

15 Penultimately preferred compounds of the formula (Ia) are those wherein:

20  $R_1$  is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

25  $R_b$  is selected from the group consisting of, pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy and carboxy,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of methoxy, halogen and hydroxy;

30  $R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

35  $R_e$  is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

$R_5$  is H;

40  $R_f$  is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

45  $R_g$  is selected from the group consisting of methyl, phenyl optionally substituted by halogen; methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

R<sub>8</sub> is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

R<sub>j</sub> is selected from the group consisting of C1-5 alkyl, phenyl, piperidinyl, pyridinyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by methyl or phenyl; methoxycarbonylamino, halogen, hydroxy and carboxy, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

R<sub>k</sub> is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, methoxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by methyl or phenyl; benzyloxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-susbstituted by methyl or phenyl; halogen, hydroxy and carboxy.

Ultimately preferred compounds of the formula (Ia) are those wherein:

R<sub>1</sub> is phenyl or 4-morpholinyl, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino, R<sub>b</sub> may be further optionally substituted by a halogen atom;

R<sub>3</sub> is C1-5 alkyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

R<sub>d</sub> is selected from the group consisting of C3-6 cycloalkyl and phenyl, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of methyl and halogen;

R<sub>6</sub> is C1-5 alkyl optionally substituted by one or more R<sub>f</sub>;

R<sub>f</sub> is selected from the group consisting of C5-6 cycloalkyl, phenyl, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, and halogen, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy;

$R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

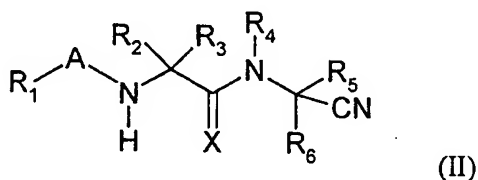
5  $R_j$  is selected from the group consisting of C1-5 alkyl, phenyl, pyridinyl, piperidinyl, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independantly mono or disubstituted by methyl or phenyl; methoxycarbonylamino and halogen,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

10  $R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, methoxycarbonyl, carbamoyl, benzyloxycarbonylamino and halogen.

15

The invention also provides novel compounds of the formula (II):

20



25

wherein:

A is  $-C(Y)-$  or  $-SO_2-$

30

Y is O, S or  $NR_a$  wherein  $R_a$  is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

35  $R_1$  is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

40  $R_b$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a



sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_2$  is H or alkyl;

$R_3$  is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_4$  is H or alkyl;

$R_5$  is H or alkyl;

R<sub>6</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

5 R<sub>f</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, heteroarylalkoxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, 10 aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or 20 more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, 25 alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein 30 the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

40 or R<sub>5</sub> together with R<sub>6</sub> form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

45 R<sub>h</sub> is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxy carbonyl, arylalkoxy carbonyl, carbamoyl wherein the nitrogen atom may

be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heteroaryl, halogen, hydroxy, carboxy and cyano;

5

X is O, S or N-OH;

with the proviso that when Y is O and R<sub>6</sub> is arylalkyl or heteroarylalkyl then R<sub>1</sub> cannot be alkyl, cycloalkyl, aryl, heteroaryl, cycloalkyl-alkyl, aryl-alkyl or aryl-cycloalkyl.

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15 Preferred compounds of the formula (II) are those wherein:

Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is H, alkyl or aryl;

20

R<sub>1</sub> is C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl, phenoxazinyl, and amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

30

R<sub>b</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxy carbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl,

45

carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxazinyl, alkoxycarbonylamino, aryloxy carbonylamino, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino;  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_3$  is H, C1-8 alkyl, C3-7 cycloalkyl, aryl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,

thiomorpholinyl, piperazinyl and indolyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>f</sub> is H, C1-8 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R<sub>f</sub> is optionally substituted by one or more R<sub>g</sub>;

R<sub>f</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8

alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxy, carbamoyl, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonamino, arylsulfonamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8

5 alkoxycarbonyl, aryloxy, carbamoyl  
 wherein the nitrogen atom may be independently mono or di-substituted  
 by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of  
 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and  
 indolinyl, or heteroaryl selected from the group consisting of furanyl,  
 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl,  
 isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,  
 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl,  
 10 isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and  
 phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein  
 the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein  
 the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein  
 either nitrogen atom may be independently substituted by alkyl, aryl,  
 15 heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or  
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl,  
 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl,  
 20 pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl,  
 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
 alkoxy-carbonylamino, aryloxy-carbonylamino, alkylcarbamoyloxy,  
 arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,  
 25 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom  
 may be independently mono or di-substituted by alkyl, aryl, heterocyclyl  
 selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 30 thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,  
 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,  
 quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen,  
 35 hydroxy, oxo, carboxy, cyano, nitro, amidino, and guanidino;

40  $R_h$  is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy-carbonyl,  
 aryloxy-carbonyl, arylC1-8alkoxy-carbonyl, carbamoyl wherein the nitrogen atom  
 may be optionally mono or di-substituted with a group selected from C1-8 alkyl,  
 C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group  
 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl  
 and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl,  
 45 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,

benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, carboxy, and cyano; and

5 X is O or S.

More preferred compounds of the formula (II) are those wherein:

10

Y is O or S;

15 R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or amino;  
20 wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

25 R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5  
30 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
35 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl,  
40 isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5



alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_2$  is H or C1-3 alkyl;

$R_3$  is H, C1-5 alkyl, C3-7 cycloalkyl, aryl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkanoyl, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,

arylamino sulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>4</sub> is H or C1-3 alkyl

R<sub>5</sub> is H or C1-8 alkyl

R<sub>6</sub> is H, C1-5 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

R<sub>f</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,

piperazinyl and indolinyl or heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,  
 pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and  
 quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5  
 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,  
 arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein  
 the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl,  
 aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected  
 from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,  
 imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl,  
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl,  
 isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy,  
 cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by  
 one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl,  
 aryl optionally substituted by one or more groups selected from halogen,  
 methyl or methoxy, heterocyclyl selected from the group consisting of  
 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and  
 indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,  
 pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and  
 quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5  
 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
 wherein the nitrogen atom may be independently mono or di-substituted  
 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of  
 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and  
 indolinyl or heteroaryl selected from the group consisting of furanyl,  
 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,  
 pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and  
 quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein  
 the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein  
 the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein  
 either nitrogen atom may be independently substituted by C1-5 alkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or  
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,  
 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl,  
 C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5  
 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,

arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino  
 wherein the nitrogen atom may be independently mono or di-substituted  
 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of  
 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and  
 indolinyl, or heteroaryl selected from the group consisting of furanyl,  
 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,  
 pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and  
 quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and  
 guanidino;

R<sub>h</sub> is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxy carbonyl,  
 aryloxy carbonyl, arylC1-5alkoxy carbonyl, carbamoyl wherein the nitrogen atom  
 may be optionally mono or di-substituted with a group selected from C1-5 alkyl,  
 C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group  
 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl  
 and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,  
 pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen,  
 hydroxy, carboxy and cyano.

Even more preferred compounds of the formula (II) are those wherein:

Y is O;

R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group  
 consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and  
 thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl; or amino wherein R<sub>1</sub> is  
 optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,  
 naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy,  
 aryloxy, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy,  
 carbamoyl wherein the nitrogen atom may be independently mono or di-  
 substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group

consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonfylamino, arylsulfonfylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy and cyano;

$R_2$  is H or methyl;

$R_3$  is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl wherein  $R_3$  is optionally substituted by one or more  $R_4$ ;

$R_4$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5  
 alkoxycarbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be  
 5 independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl,  
 heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and  
 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,  
 10 halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally  
 substituted by one or more  $R_e$ .

$R_e$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,  
 aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino,  
 15 halogen, hydroxy, oxo, carboxy and cyano;

$R_4$  is H or methyl;

20  $R_5$  is H or C1-5 alkyl;

$R_6$  is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl or cyano, wherein  $R_6$  is optionally  
 25 substituted by one or more  $R_f$ .

$R_f$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,  
 naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
 30 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl,  
 isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-  
 5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5  
 35 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be  
 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected  
 from the group consisting of piperidinyl, morpholinyl and piperazinyl or  
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,  
 40 aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a  
 sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a  
 sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized  
 to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
 45 independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the  
 group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5  
 alkoxycarbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
 5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be  
 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected  
 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and  
 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
 10 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,  
 halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally  
 substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl,  
 phenyl optionally substituted by one or more groups selected from  
 halogen, methyl or methoxy, naphthyl optionally substituted by one or  
 more groups selected from halogen, methyl or methoxy, heterocyclyl  
 selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
 20 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,  
 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl,  
 C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl,  
 25 aryloxy carbonyl, C1-5 alkanoyloxy, aryloxy, carbamoyl wherein the  
 nitrogen atom may be independently mono or di-substituted by C1-5 alkyl,  
 aryl, heterocyclyl selected from the group consisting of piperidinyl,  
 morpholinyl and piperazinyl or heteroaryl selected from the group  
 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
 30 pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,  
 aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a  
 sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a  
 sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
 35 independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from  
 the group consisting of piperidinyl, morpholinyl and piperazinyl or  
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,  
 40 C1-5 alkoxycarbonylamino, aryloxy carbonylamino, C1-5  
 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,  
 arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino  
 wherein the nitrogen atom may be independently mono or di-substituted  
 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of  
 45 pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;

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$R_h$  is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, arylC1-3alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano; and

15

X is O.

20

Yet even more preferred compounds of the formula (II) are those wherein:

Y is O;

25

$R_1$  is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

30

$R_b$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be

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independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5  
alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5  
alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,  
arylamino'sulfonyl, amino wherein the nitrogen atom may be independently mono  
or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocyclyl selected from the  
group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl  
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy,  
oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  
 $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl,  
aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

$R_2$  is H;

$R_3$  is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one  
or more  $R_4$ ;

$R_4$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl,  
naphthyl, heterocyclyl selected from the group consisting of piperidinyl,  
morpholinyl and piperazinyl; heteroaryl selected from the group consisting of  
furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and  
isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl,  
aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen  
atom may be independently mono or di-substituted by C1-5 alkyl, phenyl,  
naphthyl, heterocyclyl selected from the group consisting of piperidinyl,  
morpholinyl and piperazinyl or heteroaryl selected from the group consisting of  
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,  
C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be  
oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be  
oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group  
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl  
and indolyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy,  
arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein  
the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl,  
phenyl, heterocyclyl selected from the group consisting of piperidinyl,  
morpholinyl and piperazinyl or heteroaryl selected from the group consisting of  
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,  
halogen, hydroxy, oxo, carboxy and cyano,  $R_4$  may be further optionally  
substituted by one or more  $R_c$ ;

R<sub>c</sub> is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

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R<sub>4</sub> is H;

10 R<sub>6</sub> is H, C1-5 alkyl, C3-6 cycloalkyl, phenyl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

R<sub>f</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group  
15 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, heteroarylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5  
20 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may  
25 be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and  
30 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

35 R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the  
40 group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, C1-5  
45 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom

5 may be independently substituted by C1-5 alkyl or aryl, C1-5  
alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,  
arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom  
may be independently mono or di-substituted by C1-5 alkyl or aryl,  
halogen, hydroxy, oxo, carboxy and cyano;

10  $R_h$  is selected from the group consisting of C1-5 alkyl, phenyl, C1-5  
alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein  
the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6  
cycloalkyl, phenyl, naphthyl or arylC1-3alkyl; halogen, hydroxy, carboxy and  
cyano.

15

Still yet even more preferred compounds of the formula(II) are those wherein:

20  $R_i$  is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group  
consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl  
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,  
imidazolyl, pyridinyl and indolyl or amino, wherein  $R_i$  is optionally substituted by one or  
more  $R_b$ ;

25

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl,  
heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and  
piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl,  
pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
30 benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3  
alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
wherein the nitrogen atom may be independently mono or di-substituted by C1-3  
alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl,  
imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and  
35 benzthiazolyl C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur  
atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom  
may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom  
may be independently substituted by C1-3alkyl or phenyl, C1-5  
alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be  
40 independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected  
from the group consisting of piperidinyl, morpholinyl and piperazinyl or  
heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl,  
indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl  
and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further  
45 optionally substituted by one or more  $R_c$ ;

R<sub>c</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

5 R<sub>3</sub> is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

10 R<sub>d</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5  
15 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

20 R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

25 R<sub>5</sub> is H or C1-3alkyl;

R<sub>6</sub> is H, C1-5 alkyl, phenyl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

30 R<sub>f</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-3  
35 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

40 R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from the group consisting of halogen and methyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy,  
45

aryloxy, benzyloxy, C1-5 alkoxy, carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxy, carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy, carbonyl, phenoxy, carbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from the group consisting of C1-5 alkyl, phenyl and benzyl, halogen, hydroxy, carboxy and cyano.

Even more preferred compounds of the formula (II) are those wherein:

$R_1$  is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxy, carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

$R_3$  is C1-5 alkyl, C5-6 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more groups of the formula  $R_d$ ;

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, C1-5 alkoxy, carbonyl, C1-5 alkanoyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5

alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy-carbonylamino, C1-3 alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

wherein the configuration at the stereocenter defined by  $R_2$  and  $R_3$  and the carbon they are attached to is defined as L;

$R_5$  is H or methyl;

$R_6$  is C1-5 alkyl, phenyl or cyano wherein  $R_6$  is optionally substituted by one or more groups of the formula  $R_f$ ;

$R_f$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy-carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxy-carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy-carbonyl, benzyloxy and carboxy.

Much more preferred compounds of formula (II) are those wherein:

$R_1$  is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranlyl, thiopyranlyl or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl,

5 benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

10  $R_c$  is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy,

$R_3$  is C1-5 alkyl or C5-6 cycloalkyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

15  $R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

20  $R_e$  is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

25  $R_6$  is C1-5 alkyl or phenyl, wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

30  $R_f$  is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

35  $R_g$  is selected from the group consisting of methyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy and carboxy;

40

$R_h$  is selected from the group consisting of vinyl, phenyl, methoxycarbonyl, benzyloxycarbonyl and carboxy;

45

Penultimately preferred compounds of the formula (II) are those wherein:

- 5 R<sub>1</sub> is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranlyl or thiopyranlyl, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

10 R<sub>b</sub> is selected from the group consisting of pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy and carboxy, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of methoxy, halogen and hydroxy;

15 R<sub>d</sub> is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

20 R<sub>e</sub> is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

R<sub>5</sub> is H;

25 R<sub>f</sub> is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

30 R<sub>g</sub> is selected from the group consisting of methyl, phenyl optionally substituted by halogen, methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

35 R<sub>h</sub> is vinyl or phenyl.

40 Ultimately preferred compounds of formula (II) are those wherein:

R<sub>1</sub> is phenyl, naphthyl or 4-morpholinyl wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;



$R_b$  is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino  $R_b$  may be further optionally substituted by  $R_c$  wherein  $R_c$  is a halogen atom;

5

$R_3$  is C1-5 alkyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

10

$R_d$  is selected from the group consisting of C3-6 cycloalkyl, phenyl or naphthyl,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of methyl and halogen,

15

$R_f$  is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, indolyl, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen and carboxy,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

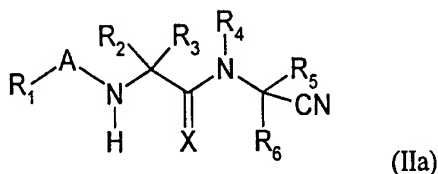
20

$R_g$  is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy.

25

In another embodiment of the invention, there are provided compounds of the formula (IIa):

30



wherein:

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A is -C(Y)- or -SO<sub>2</sub>-

Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

40

R<sub>1</sub> is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

5 R<sub>b</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino; R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

20 R<sub>c</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R<sub>2</sub> is H or alkyl;

R<sub>3</sub> is H, C2-8alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

30 R<sub>d</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5

R<sub>4</sub> is H or alkyl;

R<sub>5</sub> is H or alkyl;

10

R<sub>6</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

15

R<sub>f</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, heteroarylalkoxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

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R<sub>g</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl,

aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

- 5 or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

R<sub>h</sub> is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxy carbonyl, arylalkoxycarbonyl, carbamoyl wherein the nitrogen atom may  
10 be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heteroaryl, halogen, hydroxy, carboxy and cyano;

X is O, S or N-OH;

- 15 and the pharmaceutically acceptable salts, esters or tautomers thereof;

with the following provisos:

- 20 when Y is O and R<sub>6</sub> is arylalkyl or heteroarylalkyl then R<sub>1</sub> cannot be alkyl, cycloalkyl, aryl, heteroaryl, cycloalkyl-alkyl, aryl-alkyl or aryl-cycloalkyl;

when R<sub>5</sub> is H then R<sub>6</sub> cannot be H;  
and

- 25 when R<sub>1</sub> is C1alkyl then R<sub>6</sub> cannot be carbamoyl, alkanoylamino, aroylamino, ureido, alkoxycarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, amino, amidino or guanidino wherein each said R<sub>6</sub> is linked to said R<sub>1</sub> via the nitrogen atom thereof.

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Preferred compounds of the formula (IIa) are those wherein:

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Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is H, alkyl or aryl;

- 40 R<sub>1</sub> is C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl,  
45 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl, phenoxazinyl, and amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

5  $R_b$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl or phenoxazinyl, C1-8 alkoxo, aryloxy, C1-8 alkoxycarbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl or phenoxazinyl, alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino;  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

45  $R_c$  is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>3</sub> is H, C2-8 alkyl, C3-7 cycloalkyl, aryl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>4</sub>;

R<sub>4</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl

and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

5  $R_e$  is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

10  $R_f$  is H, C1-8 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein  $R_f$  is optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl

selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,



5 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinoliny, isoquinoliny, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, and guanidino;

10 or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>n</sub>;

15 R<sub>n</sub> is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy carbonyl, aryloxy carbonyl, arylC1-8alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinoliny, isoquinoliny, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, carboxy, and cyano; and

25 X is O or S.

30 More preferred compounds of the formula (IIa) are those wherein:

Y is O or S;

35 R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny, isoquinoliny, quinazolinyl and quinoxaliny or amino; wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

45 R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl

selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny,  
 isoquinoliny, quinazoliny and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5  
 5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
 wherein the nitrogen atom may be independently mono or di-substituted by C1-8  
 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 10 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny,  
 isoquinoliny, quinazoliny and quinoxaliny, C1-5 alkanoylamino, aroylamino,  
 C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone,  
 arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido  
 15 wherein either nitrogen atom may be independently substituted by alkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected  
 from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,  
 imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl,  
 20 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny,  
 isoquinoliny, quinazoliny and quinoxaliny, C1-5 alkoxycarbonylamino,  
 aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5  
 alkylsulfonfylamino, arylsulfonfylamino, C1-5 alkylaminosulfonfyl,  
 arylaminosulfonfyl, amino wherein the nitrogen atom may be independently mono  
 or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of  
 25 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl,  
 or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,  
 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
 30 quinoliny, isoquinoliny, quinazoliny and quinoxaliny, halogen, hydroxy, oxo,  
 carboxy, cyano, nitro, amidino and guanidino,  $R_b$  may be further optionally  
 substituted by one or more  $R_c$ ;

35  $R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,  
 aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro,  
 amidino and guanidino;

$R_2$  is H or C1-3 alkyl;

40  $R_3$  is H, C2-5 alkyl, C3-7 cycloalkyl, aryl wherein  $R_3$  is optionally substituted by one or  
 more  $R_d$ ;

45  $R_d$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from  
 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,

triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl,  
 quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5alkanoyl, aroyl, C1-5  
 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
 5 wherein the nitrogen atom may be independently mono or di-substituted by C1-5  
 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
 10 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl,  
 isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino,  
 C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone,  
 arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido  
 wherein either nitrogen atom may be independently substituted by C1-5 alkyl,  
 15 aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected  
 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
 triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl,  
 20 quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino,  
 aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5  
 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,  
 arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono  
 or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group  
 25 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl  
 and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,  
 pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen,  
 30 hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_d$  may be further  
 optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,  
 aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino,  
 35 halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_d$  is H or C1-3 alkyl  
 40

$R_5$  is H or C1-8 alkyl

45  $R_6$  is H, C1-5 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein  $R_6$  is optionally substituted  
 by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,

5 benzimidazolyl, benzthiazolyl, quinoliny, isoquinoliny, quinazoliny and  
 quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5  
 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
 wherein the nitrogen atom may be independently mono or di-substituted  
 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of  
 10 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and  
 indolinyl or heteroaryl selected from the group consisting of furanyl,  
 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,  
 pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
 15 benzimidazolyl, benzthiazolyl, quinoliny, isoquinoliny, quinazoliny and  
 quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein  
 the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein  
 the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein  
 either nitrogen atom may be independently substituted by C1-5 alkyl, aryl,  
 20 heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or  
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,  
 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 25 benzthiazolyl, quinoliny, isoquinoliny, quinazoliny and quinoxaliny,  
 C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5  
 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,  
 arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino  
 wherein the nitrogen atom may be independently mono or di-substituted  
 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of  
 30 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and  
 indolinyl, or heteroaryl selected from the group consisting of furanyl,  
 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,  
 pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinoliny, isoquinoliny, quinazoliny and  
 quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and  
 guanidino;

35 or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 6  
 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>n</sub>;

40 R<sub>n</sub> is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl,  
 aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom  
 may be optionally mono or di-substituted with a group selected from C1-5 alkyl,  
 C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group  
 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl  
 and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,  
 45 pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, quinoliny, isoquinoliny, quinazoliny and quinoxaliny, halogen,  
 hydroxy, carboxy and cyano.

5 Even more preferred compounds of the formula (IIa) are those wherein:

Y is O;

10 R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl; or amino wherein R<sub>1</sub> is  
15 optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
20 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-  
25 substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5  
30 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5  
35 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
40 oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

45 R<sub>c</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy and cyano;

R<sub>2</sub> is H or methyl;

5 R<sub>3</sub> is H, C2-5 alkyl, C3-7 cycloalkyl or phenyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

10 R<sub>d</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, 15 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or 20 heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, 25 halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

30 R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

R<sub>4</sub> is H or methyl;

45 R<sub>5</sub> is H or C1-5 alkyl;

R<sub>6</sub> is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>.

5 R<sub>f</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
 10 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be  
 15 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a  
 20 sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the  
 25 group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
 30 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
 35 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

40 R<sub>g</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen, methyl or methoxy, naphthyl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl  
 45 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,



pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the  
 5 nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 10 benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from  
 15 the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted  
 20 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;

30 or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>n</sub>;

R<sub>n</sub> is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein  
 35 the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
 40 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano; and

X is O.

45

Yet even more preferred compounds of the formula (IIa) are those wherein:

5 Y is O;

R<sub>1</sub> is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl or amino, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

15 R<sub>b</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxycarbonyl, aryloxy, C1-5 alkanoyloxy, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl or naphthyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

40 R<sub>c</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

R<sub>2</sub> is H;

45 R<sub>3</sub> is C2-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

5  $R_4$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxy, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_4$  may be further optionally substituted by one or more  $R_6$ ;

25  $R_6$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

30  $R_4$  is H;

$R_6$  is H, C1-5 alkyl, C3-6 cycloalkyl, phenyl or cyano, wherein  $R_6$  is optionally substituted by one or more  $R_6$ ;

35  $R_f$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, heteroarylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxy, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be

oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxy, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl, C1-5 alkoxycarbonylamino, aryloxy, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, halogen, hydroxy, oxo, carboxy and cyano;

or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

R<sub>h</sub> is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxycarbonyl, aryloxy, C1-5 alkylcarbamoyloxy, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl or arylC1-3alkyl; halogen, hydroxy, carboxy and cyano.

Still yet even more preferred compounds of the formula(IIa) are those wherein:

R<sub>1</sub> is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl or amino, wherein R<sub>1</sub> is optionally substituted by one or  
5 more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl,  
10 pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl,  
15 imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl, C1-5  
20 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl  
25 and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;  
30  
R<sub>3</sub> is C2-5 alkyl, C5-6 cycloalkyl or phenyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

R<sub>d</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a  
40 sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more  
45 R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

5 R<sub>5</sub> is H or C1-3alkyl;

R<sub>6</sub> is H, C1-5 alkyl, phenyl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

10 R<sub>f</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
15 wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-3  
20 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from the group consisting of  
25 halogen and methyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-  
30 5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino  
35 wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

40 or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

R<sub>h</sub> is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the  
45 nitrogen atom may be optionally mono or di-substituted with a group selected from the group consisting of C1-5 alkyl, phenyl and benzyl, halogen, hydroxy, carboxy and cyano.

5 Even more preferred compounds of the formula (IIa) are those wherein:

10  $R_1$  is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

15  $R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5  
20 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3alkyl, C1-3alkoxy, halogen and hydroxy;

25  $R_3$  is C2-5 alkyl, C5-6 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more groups of the formula  $R_d$ ;  
 $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, C1-5  
30 alkoxycarbonyl, C1-5 alkanoyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, C1-3 alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by  
35 one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

40 wherein the configuration at the stereocenter defined by  $R_2$  and  $R_3$  and the carbon they are attached to is defined as L;

$R_5$  is H or methyl;

45  $R_6$  is C1-5 alkyl, phenyl or cyano wherein  $R_6$  is optionally substituted by one or more groups of the formula  $R_f$ ;

$R_f$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ .

$R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

or  $R_5$  and  $R_6$  together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more  $R_h$ ;

$R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, benzyloxy and carboxy.

Much more preferred compounds of formula (IIa) are those wherein:

$R_1$  is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy,



R<sub>3</sub> is C2-5 alkyl or C5-6 cycloalkyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>4</sub>;

R<sub>4</sub> is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R<sub>4</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

R<sub>6</sub> is C1-5 alkyl or phenyl, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

R<sub>f</sub> is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of methyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy and carboxy;

or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

R<sub>h</sub> is selected from the group consisting of vinyl, phenyl, methoxycarbonyl, benzyloxycarbonyl and carboxy;

Penultimately preferred compounds of the formula (IIa) are those wherein:

R<sub>1</sub> is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom

may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy and carboxy,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of methoxy, halogen and hydroxy;

$R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

$R_5$  is H;

$R_f$  is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of methyl, phenyl optionally substituted by halogen, methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

or  $R_5$  and  $R_6$  together with the carbon they are attached form a carbocyclic ring of 3 carbon atoms, the carbocyclic ring being optionally substituted with one or more  $R_h$ ;

$R_h$  is vinyl or phenyl.

Ultimately preferred compounds of formula (IIa) are those wherein:

$R_1$  is phenyl, naphthyl or 4-morpholinyl wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino  $R_b$  may be further optionally substituted by  $R_c$  wherein  $R_c$  is a halogen atom;

$R_3$  is C2-5 alkyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C3-6 cycloalkyl, phenyl or naphthyl,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

5  $R_e$  is selected from the group consisting of methyl and halogen,

10  $R_f$  is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, indolyl, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen and carboxy,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

15  $R_g$  is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy and

$R_5$  and  $R_6$  together with the carbon they are attached form a carbocyclic ring of 3 carbon atoms, the carbocyclic ring being optionally substituted with one or more  $R_h$ .

20

The following are representative compounds according to the invention:

25

N-(4-morpholinecarbonyl)-L-leucine (1S-cyano-3-phenylpropyl)amide;

N-(4-morpholinecarbonyl)-L-Homophenylalanine(1S-cyano-3-phenylpropyl)amide;

30

N-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (1S-cyano-3-phenylpropyl)amide;

N-(4-morpholinecarbonyl)-L-leucine-(1S-cyano-3-phenylpropyl)-N-methylamide;

35

N-(4-Morpholinecarbonyl)-L-leucine-[1R,S(benzthiazol-2-ylcarbonyl)-3-phenylpropyl]amide;

N-[(4-Morpholinecarbonyl)-L-leucine-[1R,S-(thiazol-2-ylcarbonyl)-3-phenylpropyl]amide;

40

N-(4-Morpholinecarbonyl)-L-leucine-[1R,S-[(1-(3-N-Benzyl)imidazol-2-ylcarbonyl)-3-phenylpropyl]amide;

45

N-(4-Morpholinecarbonyl)-L-leucine-[1R,S-(2-imidazolylcarbonyl)-3-phenylpropyl]amide;

N- (4-morpholinecarbonyl)-L-leucine (cyanomethyl)amide;

- N-(4-Morpholinecarbonyl)-L-leucine [1S-cyano-5-((benzyloxycarbonyl)-amino)-pentyl]amide;
- 5    *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-3-phenylpropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-(1*S*-cyano-5-aminopentyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine-(1*S*-cyano-3-phenylpropyl)amide;
- 10    *N*-(4-morpholinecarbonyl)-L-(*p*-ethoxy)phenylalanine-(1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*S*-cyano-4-(benzyloxycarbonylamino)-butyl]amide;
- 15    *N*-(4-Morpholinecarbonyl)-L-leucine-[1-(benzthiazol-2-ylcarbonyl)-5-[(benzyloxycarbonyl)amino]-pentyl]amide;
- N*-(1-naphthylsulfonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*S*-cyano-3-phenylpropyl)amide;
- 20    *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(methanesulfonyl)-D-(*O*-benzyl)serine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-D-leucine (1*R*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-((4-dimethylaminophenyl)sulfonyl)-L-leucine (1*S*-cyano-3-(phenylpropyl))amide;
- 25    *N*-(*t*-Butoxycarbonyl)-L-leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 30    *N*-(4-methoxy-phenylsulfonyl)-L-leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,*S*-(benzoxazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 35    *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2*R*-benzyloxypropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,*S*-[(4-phenylthiazol-2-yl)-carbonyl]-3-phenylpropyl]amide;
- 40    *N*-(4-morpholinecarbonyl)-D-leucine (1*S*-cyano-3-phenylpropyl)amide;

- N*-(4-morpholinecarbonyl)-L-leucine [[1-[(6-phenylcarbamoyl)benzothiazol-2-ylcarbonyl]-3-phenylpropyl]amide;
- N*-(methylsulfonyl)-L-leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 5 *N*-(4-morpholinecarbonyl)-L-(*p*-phenyl)phenylalanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,*S*-[(5-phenylthiazol-2-yl)-carbonyl]-3-phenylpropyl]amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-chlorophenyl)methoxyethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-phenylglycine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine [1-(Benzothiazol-2-ylcarbonyl)-2-benzyloxyethyl]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[[6-(carbomethoxy)-benzoxazol-2-ylcarbonyl]-3-phenylpropyl]amide;
- 20 *N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,*S*-[(4-(4-benzyloxycarbonylamino)phenyl)thiazol-2-yl)-carbonyl]-3-phenylpropyl]amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methoxyphenyl)methoxyethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfonyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfinyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methoxyphenyl)methylsulfanyl)ethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methylphenyl)methylsulfanyl)ethyl)amide;

- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-chlorophenyl)methyloxyethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-chlorophenyl)methyloxyethyl)amide;
- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-Morpholinecarbonyl]-L-leucine 1*S*-((2-phenyloxazol-5-yl)carbonyl)-3-phenylpropylamide;
- 10 *N*-(4-morpholinecarbonyl)-L-(*p*-phenylcarbonyl)phenylalanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-methylphenyl)methyloxyethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methylphenyl)methyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-methylphenyl)methyloxyethyl)amide;
- 20 *N*-(4-Morpholinecarbonyl]-L-leucine 1*RS*-((5-phenyloxazol-2-yl)carbonyl)-3-phenylpropylamide;
- 25 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-nor-leucine (1*S*-cyano-3-phenylpropyl)amide;
- 30 *N*-(Benzyloxycarbonyl)-L-(*O*-*t*-butyl)serine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-Morpholinecarbonyl]-L-leucine 1*S*-(oxazol-2-ylcarbonyl)-3-phenylpropylamide;
- N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 35 *N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-cyclohexylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-carbomethoxyphenyl)methyloxyethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-carbomethoxyphenyl)methyloxyethyl)amide;

- N*-(4-Morpholinecarbonyl)-L-leucine 1*S*-(pyrid-2-ylcarbonyl)-3-phenylpropylamide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,*S*-[(4-(2-benzyloxyamino)phenyl-thiazol-2-yl)-carbonyl]-3-phenylpropyl]amide;
- 5 *N*-(4-morpholinecarbonyl)-L-(*O*-*t*-butyl)serine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-hydroxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbo-*t*-butoxy)propyl)amide;
- 10 *N*-(cyclohexylcarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbo-*t*-butoxy)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine dicyanomethylamide;
- N*-(4-morpholinecarbonyl)-L-(2-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-(*O*-Benzyl)glutamate (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-homo-tyrosine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-norvaline (1*S*-cyano-3-phenylpropyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-(2-chlorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-Benzoyl-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-(4,5-dehydro)leucine(1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(*O*-methyl)tyrosine(1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-iso-leucine (1*S*-cyano-3-phenylpropyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-(4-nitrophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(4-fluorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-tyrosine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(1-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-methionine (1*S*-cyano-3-phenylpropyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(1-benzyl-4-imidazolyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(1-benzyl-4-imidazolyl)ethyl)amide;

- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;  
5 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-1-phenylmethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-1-phenylmethyl)amide;  
10 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-benzyloxyphenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-benzyloxyphenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1-cyanocyclopropyl)amide;  
15 *N*-(4-morpholinecarbonyl)-L-leucine (1-cyanocyclopropyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-phenylphenyl)ethyl)amide;  
20 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-phenylphenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-benzoylphenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(4-benzoylphenyl)ethyl)amide;  
25 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(1-naphthyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(1-naphthyl)ethyl)amide;  
30 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-naphthyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-naphthyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;  
35 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-chlorophenyl)ethyl)amide;  
40 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-chlorophenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3,4-dichlorophenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3,4-dichlorophenyl)ethyl)amide;  
45 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanobut-3-ynyl)amide;



- N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyanobut-3-ynyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanopropyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-phenylalanine;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-(2,6-dichloromethyloxy)phenyl)ethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2*S*-methylbutyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanopentyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanopentyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2,2-dimethylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2,2-dimethylpropyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-methylbutyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-methylbutyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-nitrophenylethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-nitrophenylethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanobutyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanobutyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*R*-cyano-2*R*-benzyloxypropyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanoethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanoethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3-benzimidazolyl)ethyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3-benzimidazolyl)ethyl)amide;

- N*-(4-morpholinecarbonyl)-L-phenylalanine (1-cyano-1-methylethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1-cyano-1-methylethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-hydroxyphenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-hydroxyphenyl)ethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*,3-dicyanopropyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*,3-dicyanopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-hydroxy-3-iodophenyl)ethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-hydroxy-3-iodophenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*,2-dicyanoethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*,2-dicyanoethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*R*-cyano-2-benzyloxyethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-thienyl)ethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-thienyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-phenylethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-phenylethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-cyclohexylethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-cyclohexylethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3-chlorophenyl)ethyl)amide;
- 45 and  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3-chlorophenyl)ethyl)amide.

Preferred compounds of the invention include:

- 5 *N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-3-phenylpropyl)amide;  
*N*-(1-naphthylsulfonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;  
*N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*S*-cyano-3-phenylpropyl)amide;  
10 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;  
*N*-((4-dimethylaminophenyl)sulfonyl)-L-leucine (1*S*-cyano-3-(phenylpropyl))amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2*R*-benzyloxypropyl)amide;  
15 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-chlorophenyl)methoxyethyl)amide;  
*N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;  
20 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methoxyphenyl)methoxyethyl)amide;  
25 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfonyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfinyl)ethyl)amide;  
30 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methoxyphenyl)methylsulfanyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methylphenyl)methylsulfanyl)ethyl)amide;  
35 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-chlorophenyl)methoxyethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-chlorophenyl)methoxyethyl)amide;  
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- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-methylphenyl)methyloxyethyl)amide;
- 5    *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methylphenyl)methyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-methylphenyl)methyloxyethyl)amide;
- 10    *N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-cyclohexylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-carbomethoxyphenyl)methyloxyethyl)amide;
- 15    *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-carbomethoxyphenyl)methyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-hydroxyethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbo-*t*-butoxy)propyl)amide;  
*N*-(cyclohexylcarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbo-*t*-butoxy)ethyl)amide;
- 20    *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-Homophenylalanine(1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (cyanomethyl)amide;
- 30    *N*-(4-Morpholinecarbonyl)-L-leucine [1*S*-cyano-5-((benzyloxycarbonyl)-amino)-pentyl]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-(1*S*-cyano-5-aminopentyl)amide;
- 35    *N*-(4-morpholinecarbonyl)-L-phenylalanine-(1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(*p*-ethoxy)phenylalanine-(1*S*-cyano-3-phenylpropyl)amide;
- 40    *N*-(4-Morpholinecarbonyl)-L-leucine-[1*S*-cyano-4-(benzyloxycarbonylamino)-butyl]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,*S*-(benzthiazol-2-ylcarbonyl)-3-phenylpropyl]amide;

- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,*S*-(benzoxazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 5 *N*-(4-Morpholinecarbonyl)-L-leucine-[1-(benzthiazol-2-ylcarbonyl)-5-[(benzyloxycarbonyl)amino]-pentyl]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[[6-(carbomethoxy)-benzoxazol-2-ylcarbonyl]-3-phenylpropyl]amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine [[1-[(6-phenylcarbonyl)benzothiazol-2-ylcarbonyl]-3-phenylpropyl]]amide;
- N*-(4-morpholinecarbonyl)-L-(*p*-phenyl)phenylalanine (1*S*-cyano-3-phenylpropyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-phenylglycine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*S*-cyano-3-phenylpropyl)amide;
- 20 *N*-(4-Morpholinecarbonyl)-L-leucine 1*S*-((2-phenyloxazol-5-yl)carbonyl)-3-phenylpropylamide;
- N*-(4-morpholinecarbonyl)-L-(*p*-phenylcarbonyl)phenylalanine (1*S*-cyano-3-phenylpropyl)amide;
- 25 *N*-(4-Morpholinecarbonyl)-L-leucine 1*RS*-((5-phenyloxazol-2-yl)carbonyl)-3-phenylpropylamide;
- N*-(4-Morpholinecarbonyl)-L-leucine 1*S*-(oxazol-2-ylcarbonyl)-3-phenylpropylamide;
- 30 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-nor-leucine (1*S*-cyano-3-phenylpropyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine 1*S*-(pyrid-2-ylcarbonyl)-3-phenylpropylamide;
- 40 *N*-(4-morpholinecarbonyl)-L-(*O*-*t*-butyl)serine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-(2-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(*O*-Benzyl)glutamate (1*S*-cyano-3-phenylpropyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-homo-tyrosine (1*S*-cyano-3-phenylpropyl)amide;

- N*-(4-morpholinecarbonyl)-L-norvaline (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(2-chlorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 5 *N*-Benzoyl-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-(4,5-dehydro)leucine(1*S*-cyano-3-phenylpropyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-(*O*-methyl)tyrosine(1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-iso-leucine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(4-nitrophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-(4-fluorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-tyrosine (1*S*-cyano-3-phenylpropyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-(1-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-methionine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(1-benzyl-4-imidazolyl)ethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(1-benzyl-4-imidazolyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-1-phenylmethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-1-phenylmethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-benzyloxyphenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-benzyloxyphenyl)ethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1-cyanocyclopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1-cyanocyclopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-phenylphenyl)ethyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-phenylphenyl)ethyl)amide;

- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-benzoylphenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(4-benzoylphenyl)ethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(1-naphthyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(1-naphthyl)ethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-naphthyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-naphthyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-chlorophenyl)ethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-chlorophenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3,4-dichlorophenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3,4-dichlorophenyl)ethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanobut-3-ynyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyanobut-3-ynyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-(2,6-dichloromethyloxy)phenyl)ethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-(2,6-dichloromethyloxy)phenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2*S*-methylbutyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanopentyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanopentyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2,2-dimethylpropyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2,2-dimethylpropyl)amide;

- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-methylbutyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-methylbutyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-nitrophenylethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-nitrophenylethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanobutyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanobutyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*R*-cyano-2*R*-benzyloxypropyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanoethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanoethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3-benzimidazolyl)ethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3-benzimidazolyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1-cyano-1-methylethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (1-cyano-1-methylethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-hydroxyphenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-hydroxyphenyl)ethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*,3-dicyanopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*,3-dicyanopropyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-hydroxy-3-iodophenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-hydroxy-3-iodophenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*,2-dicyanoethyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*,2-dicyanoethyl)amide;



- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*R*-cyano-2-benzyloxyethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-thienyl)ethyl)amide;  
5 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-thienyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;  
10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-phenylethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-phenylethyl)amide;  
15 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;  
20 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-cyclohexylethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-cyclohexylethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3-chlorophenyl)ethyl)amide;  
25 and  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3-chlorophenyl)ethyl)amide.

30

More preferred compounds of the invention include:

- 35 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*S*-cyano-3-phenylpropyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;  
40 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2*R*-benzyloxypropyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-chlorophenyl)methoxyethyl)amide;

- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-chlorophenyl)methyloxyethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methoxyphenyl)methyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfonyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfinyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methoxyphenyl)methylsulfanyl)ethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-chlorophenyl)methyloxyethyl)amide;
- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-methylphenyl)methyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methylphenyl)methyloxyethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-methylphenyl)methyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-carbomethoxyphenyl)methyloxyethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-carbomethoxyphenyl)methyloxyethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbo-*t*-butoxy)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*S*-(benzthiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 40 *N*-(4-Morpholinecarbonyl)-L-leucine [1*S*-cyano-5-((benzyloxycarbonyl)-amino)-pentyl]amide;

- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,S(benzoxazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine [[1-[(6-phenylcarbonyl)benzothiazol-2-ylcarbonyl]-3-phenylpropyl]]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[[6-(carbomethoxy)-benzoxazol-2-ylcarbonyl]-3-phenylpropyl]amide;
- 10 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-nor-leucine (1*S*-cyano-3-phenylpropyl)amide;
- 15 *N*-(4-Morpholinecarbonyl)-L-leucine 1*RS*-((5-phenyloxazol-2-yl)carbonyl)-3-phenylpropylamide;
- N*-(4-Morpholinecarbonyl)-L-leucine 1*S*-(oxazol-2-ylcarbonyl)-3-phenylpropylamide;
- 20 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- N*-(4-morpholinecarbonyl)-L-(2-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-(2-chlorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-Benzoyl-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-(*O*-methyl)tyrosine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-1-phenylmethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1-cyanocyclopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-(2,6-dichloromethyloxy)phenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*,3-dicyanopropyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*S*,2-dicyanoethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;

5 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;

and

10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-cyclohexylethyl)amide.

15

Any compounds of this invention containing one or more asymmetric carbon atoms may occur as racemates and racemic mixtures, single enantiomers, diastereomeric mixtures and individual diastereomers. All such isomeric forms of these compounds are expressly included in the present invention. Each stereogenic carbon may be in the R or S  
20 configuration, or a combination of configurations.

Some of the compounds of formulas (I), (Ia) and formulas (II), (IIa) can exist in more than one tautomeric form. The invention includes all such tautomers.

25 It shall be understood by one of ordinary skill in the art that all compounds of the invention are those which are chemically stable.

The invention includes pharmaceutically acceptable derivatives of compounds of formulas (I), (Ia) and formulas (II), (IIa). A "pharmaceutically acceptable derivative"  
30 refers to any pharmaceutically acceptable salt or ester of a compound of this invention, or any other compound which, upon administration to a patient, is capable of providing (directly or indirectly) a compound of this invention, a pharmacologically active metabolite or pharmacologically active residue thereof. A pharmacologically active metabolite shall be understood to mean any compound of the invention capable of being  
35 metabolized enzymatically or chemically. This includes, for example, hydroxylated or oxidized derivative compounds of the invention.

In addition, the compounds of this invention include prodrugs of compounds of the formulas (I),(Ia) and formulas (II), (IIa). Prodrugs include those compounds that, upon simple chemical transformation, are modified to produce the compounds of the invention. Simple chemical transformations include hydrolysis, oxidation and reduction. Specifically, when a prodrug of this invention is administered to a patient, the prodrug may be transformed into a compound of formulas (I),(Ia) or formulas (II), (IIa), thereby imparting the desired pharmacological effect.

10

In order that the invention herein described may be more fully understood, the following detailed description is set forth. As used herein, the following abbreviations are used:

BOC or t-BOC is tertiary butoxycarbonyl;

t-Bu is tertiary butyl;

15 

DMF is dimethylformamide;

EtOAc is ethyl acetate;

THF is tetrahydrofuran;

Ar is argon;

TFA is trifluoroacetic acid;

20 

EDC is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride.

HOBT is 1-hydroxybenzotriazole

Also, as used herein, each of the following terms, used alone or in conjunction with other terms, are defined as follows (except where noted to the contrary):

25

The term "alkyl" refers to a saturated aliphatic radical containing from one to ten carbon atoms or a mono- or polyunsaturated aliphatic hydrocarbon radical containing from two to twelve carbon atoms, containing at least one double or triple bond, respectively.

30 

"Alkyl" refers to both branched and unbranched alkyl groups. Preferred alkyl groups are straight chain alkyl groups containing from one to eight carbon atoms and branched alkyl groups containing from three to eight carbon atoms. More preferred alkyl groups are

straight chain alkyl groups containing from one to six carbon atoms and branched alkyl groups containing from three to six carbon atoms. It should be understood that any combination term using an "alk" or "alkyl" prefix refers to analogs according to the above definition of "alkyl". For example, terms such as "alkoxy", "alkythio" refer to  
5 alkyl groups linked to a second group via an oxygen or sulfur atom. "Alkanoyl" refers to an alkyl group linked to a carbonyl group (C=O).

The term "cycloalkyl" refers to the cyclic analog of an alkyl group, as defined above.  
10 Preferred cycloalkyl groups are saturated cycloalkyl groups containing from three to eight carbon atoms, and more preferably three to six carbon atoms.

The term "aryl" refers to phenyl and naphthyl. "Aroyl" refers to an aryl group linked to a  
15 carbonyl group (C=O).

The term "halo" refers to a halogen radical selected from fluoro, chloro, bromo or iodo. Preferred halo groups are fluoro, chloro and bromo.

20 The term "heteroaryl" refers to a stable 5-8 membered (but preferably, 5 or 6 membered) monocyclic or 8-11 membered bicyclic aromatic heterocycle radical. Each heterocycle consists of carbon atoms and from 1 to 4 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur. As used herein, "nitrogen" and "sulfur" include any oxidized form of nitrogen and sulfur and the quaternized form of any basic nitrogen. The  
25 heterocycle may be attached by any atom of the cycle, which results in the creation of a stable structure. Preferred heteroaryl radicals include, for example, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl,  
30 benzthiazolyl, benzoxazolyl, purinyl, quinoliziny, quinoliny, isoquinoliny, cinnoliny,

phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl or phenoxazinyl,

The term "heterocycle" refers to a stable 5-8 membered (but preferably, 5 or 6  
5 membered) monocyclic or 8-11 membered bicyclic heterocycle radical which may be  
either saturated or unsaturated, and is non-aromatic. Each heterocycle consists of carbon  
atoms and from 1 to 4 heteroatoms selected from the group consisting of nitrogen,  
oxygen and sulfur. As used herein, "nitrogen" and "sulfur" include any oxidized form of  
nitrogen and sulfur and the quaternized form of any basic nitrogen. The heterocycle may  
10 be attached by any atom of the cycle, which results in the creation of a stable structure.  
Preferred heterocycle radicals include, for example, pyrrolinyl, pyrrolidinyl, pyrazolinyl,  
pyrazolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl,  
piperazinyl and indolinyl.

15

#### GENERAL SYNTHETIC METHODS

The invention also provides processes of making the present novel compounds.  
Compounds of the invention may be prepared by methods described below. Standard  
20 peptide coupling, protection and deprotection reactions (see for example M. Bodanszky,  
The Practice of Peptide Synthesis, Springer-Verlag, 1984) are employed in these  
syntheses.

Compounds of the invention having formula (II) or (IIa) (nitriles) may be prepared by  
25 Method A (Scheme I)

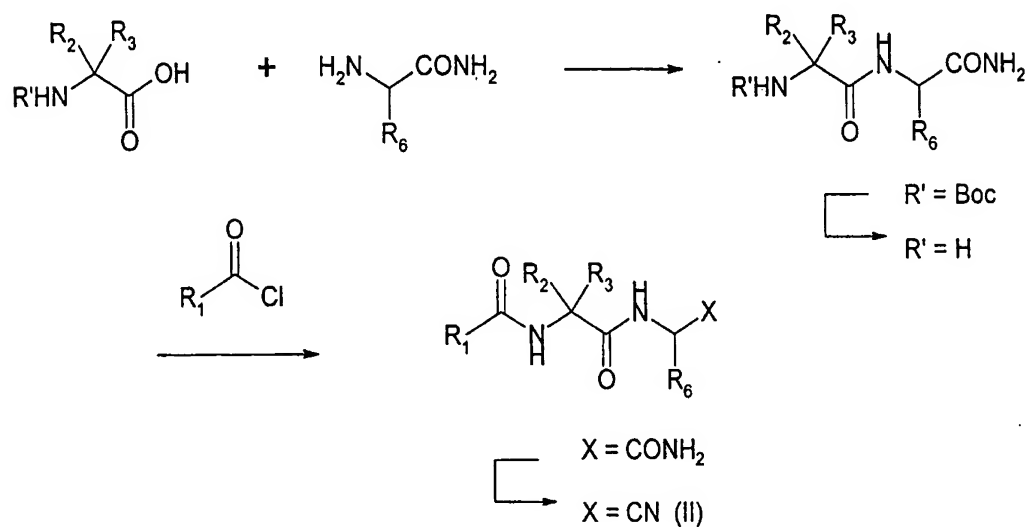
Scheme I (Method A)





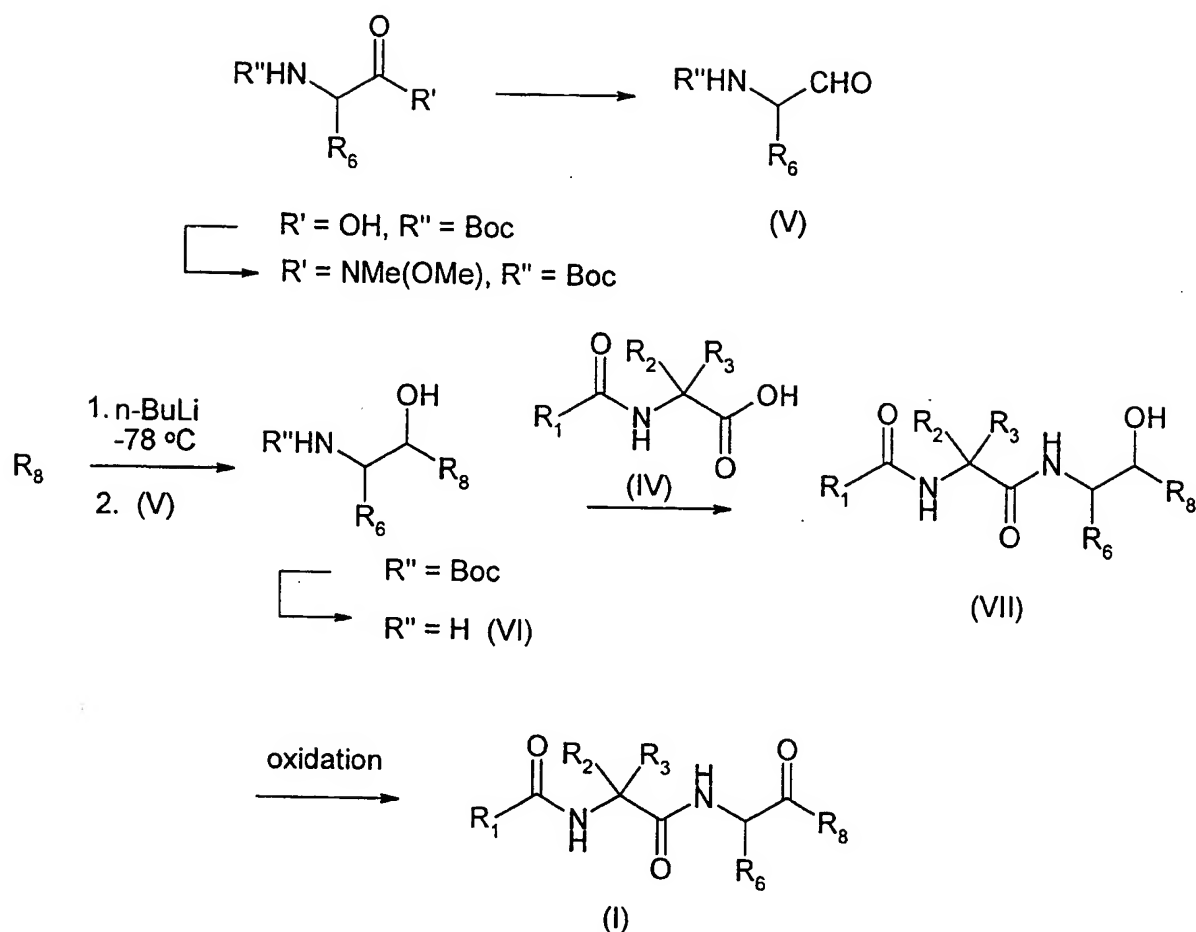
In a variation (Method B) illustrated in Scheme II, an amino acid amide bearing  $R_6$  is coupled with an amine-protected amino acid bearing  $R_2$  and  $R_3$ . A suitable protecting group and coupling conditions would be as described above. Deprotection is then followed by reaction with an acid chloride bearing  $R_1$ . Conversion of the amide to the nitrile as above provides II or IIa.

### Scheme II (Method B)



Compounds of the invention having formulas (I) or (Ia) (ketones) may be prepared by Methods C (Scheme III) or D (Scheme IV) as described below.

### Scheme III (Method C)

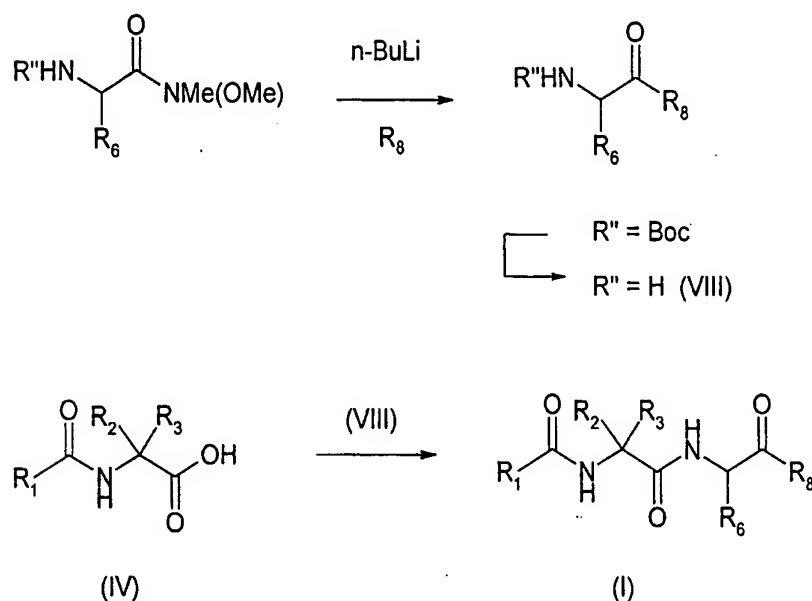


- According to Method C, a suitably protected (for example Boc protected) amino acid is coupled with N,O-dimethylhydroxylamine under standard coupling conditions, such as with carbonyldiimidazole (CDI) in a solvent such as DMF, to give the corresponding amide. This is reduced to the aldehyde (V) with a suitable reducing agent such as  $\text{LiAlH}_4$ , in a suitable solvent such as THF.
- The aldehyde (V) is reacted with the anion of a heterocycle  $R_8$ , which is generated by reacting  $R_8$  with a strong base such as  $n\text{-BuLi}$  in a solvent such as THF at a temperature of about  $-30^\circ\text{C}$  to  $-100^\circ\text{C}$  and preferably at about  $-78^\circ\text{C}$ . This is followed by removal of the protecting group providing alcohol (VI). This is coupled with (IV), prepared as described in Scheme 1, under standard coupling conditions such as EDC and HOBT in

DMF in the presence of a base such as N-methylmorpholine to provide (VII). Oxidation of (VII) with, for example, the Dess Martin Reagent (1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1H)-one) in methylene chloride and t-BuOH, provides the desired ketone of formulas (I) or (Ia).

5

## Scheme IV (Method D)



- 10 In Method D, a suitably protected amino acid N-methoxy-N-methylamide (prepared as described in Scheme III) is treated with the anion of a heterocycle  $\text{R}_8$ , generated by reacting  $\text{R}_8$  with a strong base such as  $n\text{-BuLi}$  in a suitable solvent such as THF at a temperature of about  $-30^\circ\text{C}$  to  $-100^\circ\text{C}$  and preferably at about  $-78^\circ\text{C}$ . Deprotection of the resulting ketone provides (VIII). This is coupled with (IV), which is prepared as
- 15 described in Scheme I, under standard coupling conditions such as EDC and HOBT in DMF in the presence of a base such as N-methylmorpholine to provide the desired ketone of formulas (I) or (Ia).

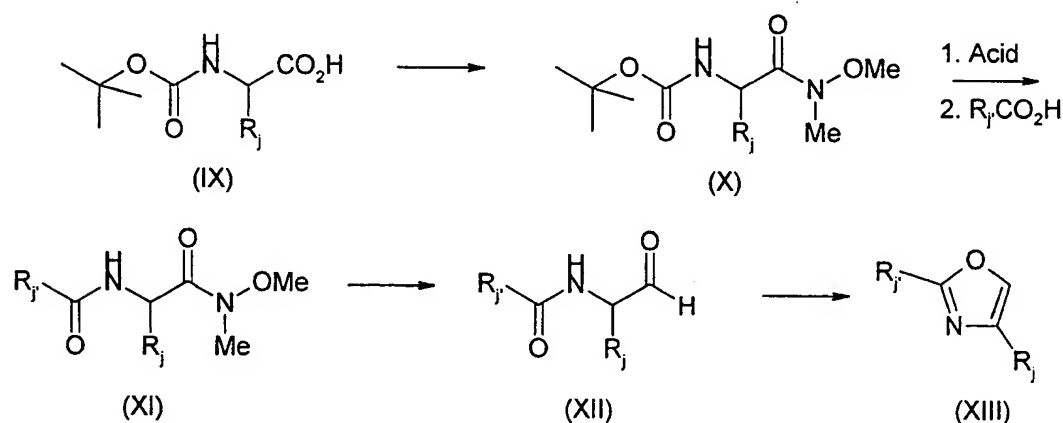
Compounds of the invention where A is a bond (formulas I, Ia and II, IIa) could be

20 prepared in analogous fashion to the Schemes above by using  $\text{R}_1\text{X}$ , where  $\text{X} = \text{Br}, \text{Cl}$ , or

I, instead of an acyl halide ( $R_1C(O)Cl$ ) in Schemes I and II, or by using  $R_1NHC(R_2)(R_3)CO_2H$  instead of (IV) in Schemes III and IV.

Intermediates used in Schemes I-IV are either commercially available or easily prepared by methods known to those skilled in the art. A procedure (Method E) that is useful for preparing substituted oxazoles which may be used as  $R_8$  in Scheme III and IV (Methods C and D) is illustrated below in Scheme V.

Scheme V (Method E)



An N-protected amino acid, for example a *t*-Boc protected amino acid (IX) is coupled with N,O-dimethylhydroxylamine using a suitable coupling agent, such as carbonyldiimidazole (CDI), in a suitable solvent, such as  $CH_2Cl_2$ , THF or DMF, at about 0 °C to provide (X). The N-protecting group is then removed, for example the *t*-Boc group may be removed by treatment with a suitable acid, such as trifluoroacetic acid, in a suitable solvent, such as  $CH_2Cl_2$ . The resulting amine is coupled with the desired carboxylic acid using suitable coupling conditions, such as EDC with HOBT in a suitable solvent such as DMF, in the presence of a base such as N-methylmorpholine to provide a diamide (XI). The N-methoxy-methyl amide is then treated with a suitable reducing agent, such as  $LiAlH_4$  in a suitable solvent, such as THF, to provide an aldehyde (XII). Cyclodehydration (see for example P. Wipf and S. Lim, J. Amer. Chem. Soc., 1995, 117, 558) of (XII) with triphenylphosphine and hexachloroethane in a suitable solvent, such

as acetonitrile in the presence of a suitable base, such as Et<sub>3</sub>N provides the desired oxazole (XIII).

Desired disubstituted thiazoles, which may be used as R<sub>8</sub> in Scheme III and IV (Method  
5 C and D) may be prepared by the Hantzsch method in which a thioamide is condensed  
with an alpha-halocarbonyl compound. This method is known to those skilled in the art  
and is well- documented in the chemical literature (for example, J. Metzger and E.J.  
Vincent, The Chemistry of Heterocyclic Compounds, Vol. 34, 1979; A.R. Katritzky et  
al., J. Org. Chem., 1995, 60, 5638; R. Flaig and H. Hartmann, Heterocycles, 1997, 45,  
10 875).

#### METHODS OF THERAPEUTIC USE

15 The compounds of this invention effectively block degradation of the invariant chain to  
CLIP by cathepsin S, and thus inhibit antigen presentation and antigen-specific immune  
responses. Control of antigen specific immune responses is an attractive means for  
treating autoimmune diseases and other undesirable T-cell mediated immune responses.  
Thus, there is provided methods of treatment using the compounds of this invention for  
20 such conditions. These encompass autoimmune diseases including, but not limited to,  
rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease, ulcerative colitis,  
multiple sclerosis, Guillain-Barre syndrome, psoriasis, Grave's disease, myasthenia  
gravis, scleroderma, glomerulonephritis, atopic dermatitis and insulin-dependent diabetes  
mellitus. The compounds of the invention can also be used to treat other disorders  
25 associated with extracellular proteolysis such as Alzheimer's disease. The compounds of  
the invention can also be used to treat other disorders associated with inappropriate  
autoimmune responses, T-cell mediated immune responses, or extracellular proteolysis  
mediated by cathepsin S, unrelated to those listed above or discussed in the Background  
of the Invention. Therefore, the invention also provides methods of modulating an  
30 autoimmune disease comprising administering to a patient in need of such treatment a  
pharmaceutically effect amount of a compound according to the invention.

For therapeutic use, the compounds of the invention may be administered in any conventional dosage form in any conventional manner. Routes of administration include, but are not limited to, intravenously, intramuscularly, subcutaneously, intrasynovially, by  
5 infusion, sublingually, transdermally, orally, topically or by inhalation. The preferred modes of administration are oral and intravenous.

The compounds of this invention may be administered alone or in combination with adjuvants that enhance stability of the inhibitors, facilitate administration of  
10 pharmaceutical compositions containing them in certain embodiments, provide increased dissolution or dispersion, increase inhibitory activity, provide adjunct therapy, and the like, including other active ingredients. Advantageously, such combination therapies utilize lower dosages of the conventional therapeutics, thus avoiding possible toxicity and adverse side effects incurred when those agents are used as monotherapies. Compounds  
15 of the invention may be physically combined with the conventional therapeutics or other adjuvants into a single pharmaceutical composition. Advantageously, the compounds may then be administered together in a single dosage form. In some embodiments, the pharmaceutical compositions comprising such combinations of compounds contain at least about 15%, but more preferably at least about 20%, of a compound of formulas (I),  
20 (Ia), (II) or (IIa) (w/w) or a combination thereof. Alternatively, the compounds may be administered separately (either serially or in parallel). Separate dosing allows for greater flexibility in the dosing regime.

As mentioned above, dosage forms of the compounds of this invention include  
25 pharmaceutically acceptable carriers and adjuvants known to those of ordinary skill in the art. These carriers and adjuvants include, for example, ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, buffer substances, water, salts or electrolytes and cellulose-based substances. Preferred dosage forms include, tablet, capsule, caplet, liquid, solution, suspension, emulsion, lozenges, syrup, reconstitutable powder, granule,  
30 suppository and transdermal patch. Methods for preparing such dosage forms are known (see, for example, H.C. Ansel and N.G. Popovich, *Pharmaceutical Dosage Forms and*

*Drug Delivery Systems*, 5th ed., Lea and Febiger (1990)). Dosage levels and requirements are well-recognized in the art and may be selected by those of ordinary skill in the art from available methods and techniques suitable for a particular patient. In some embodiments, dosage levels range from about 10-1000 mg/dose for a 70 kg patient.

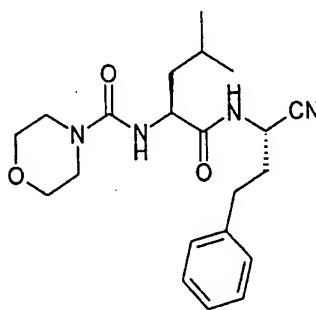
5 Although one dose per day may be sufficient, up to 5 doses per day may be given. For oral doses, up to 2000 mg/day may be required. As the skilled artisan will appreciate, lower or higher doses may be required depending on particular factors. For instance, specific dosage and treatment regimens will depend on factors such as the patient's general health profile, the severity and course of the patient's disorder or disposition  
10 thereto, and the judgment of the treating physician.

15

### SYNTHETIC EXAMPLES

#### EXAMPLE 1

**Morpholine-4-carboxylic acid [1-(S)-(1-(S)-cyano-3-phenylpropylcarbamoyl)-3-methylbutyl] amide**  
20



As outlined generally in Scheme I (Method A), *N*-Boc-L-homophenylalanine (0.50 g, 1.79 mmol) was dissolved in 20 mL of DMF which was cooled with an ice-water bath.  
25 1-Hydroxybenzotriazole (HOBT) (0.29 g, 2.14 mmol) and EDC (0.41 g, 2.00 mmol)

were added followed by stirring for 20 min. Ammonium hydroxide was added (0.5 mL) and stirring was continued overnight (16 h). The reaction mixture was diluted with 50 mL of methylene chloride to give a white precipitate. The mixture was filtered and the filtrate was washed with brine (100 mL) followed by saturated bicarbonate (100 mL).

- 5 The organic layer was dried over  $\text{MgSO}_4$ , filtered and concentrated by rotary evaporation to give the corresponding amide (0.45 g, 90%) that was used without further purification.

- Benzyl L-leucine p-toluenesulfonate salt (8.00 g, 20.3 mmol) was dissolved in 20 mL of DMF followed by addition of N,N-diisopropylethylamine (10.61 mL, 60.9 mmol) and stirring under Ar for 15 min. 4-Morpholinecarbonyl chloride (4.55 g, 30.4 mmol) was added and stirring was continued overnight (16 h). The solution was diluted with 500 mL of EtOAc and washed with 3 x 500 mL of water. The organic layer was dried over  $\text{MgSO}_4$ , filtered and concentrated by rotary evaporation to 8.01 g of the crude product. The product was purified by flash chromatography ( $\text{SiO}_2$ , 40% EtOAc/hexane) resulting in a thick oil. This oil (18 g, 53.8 mmol) was dissolved in ethanol (500 mL).  $\text{Pd}(\text{OH})_2$  (642 mg) was added followed by cyclohexene (100 mL). The mixture was refluxed for 45 min at which time TLC indicated consumption of the benzyl ester. The reaction was cooled and filtered through diatomaceous earth and evaporated to dryness to give N-(4-morpholinecarbonyl)-L-leucine as a very thick oil (13 g, 99%) that was used without further purification.
- 10  
15  
20

- N-Boc-L-homophenylalaninamide (from the first paragraph) (114 mg, 0.41 mmol) was dissolved in 10 mL of  $\text{CH}_2\text{Cl}_2$  and 10 mL of trifluoroacetic acid (TFA) was added. Stirring was continued for 30 min at which time the reaction mixture was evaporated to dryness giving the TFA salt of L-homophenylalanine amide. N-(4-morpholinecarbonyl)-L-leucine (100 mg, 0.41 mmol), from above, was dissolved in 10 mL of DMF and cooled by an ice-water bath. HOBt (72 mg, 0.53 mmol) and EDC (102 mg, 0.53 mmol) were added and the mixture was stirred at 0 °C for 15 min. To the cold solution was added the TFA salt of L-homophenylalaninamide as a solution in 5 mL of DMF, followed by addition of N-methylmorpholine (94  $\mu\text{L}$ , 0.86 mmol). The ice bath was removed and the reaction was stirred at ambient temperature overnight (16 h). The reaction was diluted
- 25  
30



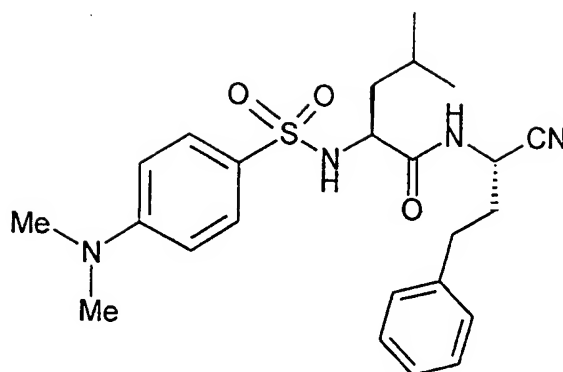
with 50 mL of CH<sub>2</sub>Cl<sub>2</sub> to give a white precipitate. The mixture was filtered and the solid washed with an additional 50 mL of CH<sub>2</sub>Cl<sub>2</sub>. The filtrates were combined and washed with saturated bicarbonate (100 mL), 1 N HCl (100 mL) and brine (2 x 100 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated by rotary evaporation to give an  
5 oily residue. The residue was chromatographed (SiO<sub>2</sub>, 5% MeOH in CH<sub>2</sub>Cl<sub>2</sub>) to give the a white solid (130 mg, 78%).

This amide (150 mg, 0.37 mmol) (material from more than one reaction) was dissolved in 2 mL of DMF and cooled to 0 °C with an ice-water bath. To the solution was added  
10 cyanuric chloride (46 mg, 0.37 mmol). The ice bath was removed and the reaction stirred to ambient temperature over the next hour. During the course of the reaction a white precipitate formed. The reaction was diluted with 100 mL of EtOAc and washed with 100 mL of water (3x). The organic layer was dried over MgSO<sub>4</sub>, filtered and concentrated by rotary evaporation to give the crude residue. The residue was purified by  
15 chromatography (SiO<sub>2</sub>, 40% hexane in EtOAc) to give the title compound as a hard white glass (120 mg, 84%). <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>): δ 8.00-7.87 (1H, m), 7.35-7.13 (3H, m), 7.12-7.05 (2H, m), 5.10-5.02 (1H, m), 4.80-4.60 (1H, m), 4.45-4.20 (1H, m), 3.75-3.50 (4H, m), 3.45-3.30 (4H, m), 2.80-2.60 (2H, m), 2.10-1.90 (2H, m), 1.70-1.45 (3H, m), 1.05-0.90 (6H, m).

20

## EXAMPLE 2

**2-(*S*)-(4-Dimethylaminobenzenesulfonylamino)-4-methylpentanoic acid (1-(*S*)-  
25 cyano-3-phenylpropyl) amide**



NH<sub>4</sub>OH (4 mL) was added to a premixed (15 min) solution of *N*-(*t*-butoxycarbonyl)-L-homophenylalanine (4.00 g, 14.3 mmol), EDC (3.24 g, 17.2 mmol), and HOBT (2.32 g, 17.2 mmol) in DMF (20 mL) at room temperature. After 16 h the reaction mixture was  
 5 diluted with CH<sub>2</sub>Cl<sub>2</sub> and filtered, washed sequentially with 10% aqueous HCl, satd. NaHCO<sub>3</sub>, H<sub>2</sub>O (×3), brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated giving *N*-(*t*-butoxycarbonyl)-L-homophenylalaninamide (3.10 g, 78%) as a white solid.

TFA (2.5 mL) was added to a solution of *N*-(*t*-butoxycarbonyl)-L-homophenylalaninamide (1.00 g, 3.59 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at room temperature.  
 10 After stirring for 0.5 h the reaction mixture was concentrated giving a colorless oil. As described generally by Scheme II, Method B, the oil was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and N,N-diisopropylethylamine (1.90 g, 14.4 mmol) and added to a premixed (15 min) solution of *N*-(*t*-butoxycarbonyl)-L-leucine (913 mg, 3.95 mmol), EDC (826 mg, 4.30  
 15 mmol), HOBT (581 mg, 4.30 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at room temperature. After stirring for 16 h the reaction was quenched by the addition of H<sub>2</sub>O, diluted with EtOAc, washed sequentially with 10% aqueous HCl, satd. NaHCO<sub>3</sub>, H<sub>2</sub>O brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated giving 1.3 g of a white solid. The crude solid was triturated with 5%EtOAc/Hexane giving *N*-[*N*-(*t*-butoxycarbonyl)-L-leuciny]-L-homophenylalaninamide (1.1 g, 78%) as a white solid.  
 20

TFA (2.5mL) was added to a solution of *N*-[*N*-(*t*-butoxycarbonyl)-L-leuciny]-L-homophenylalaninamide (500 mg, 1.28 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at room temperature. After stirring for 0.5 h the reaction mixture was concentrated giving a colorless oil which

was diluted with CH<sub>2</sub>Cl<sub>2</sub> (2.5 mL). Diisopropylethylamine (588 mg, 4.55 mmol) and *p*-Me<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Cl [prepared by the reaction of *p*-Me<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>Na<sup>+</sup> (1.0 g, 4.48 mmol) with thionyl chloride and pyridine (1 mL) at 55 °C for 2 h followed by cooling, diluting with toluene and concentrating to give *p*-Me<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Cl.] was added at room  
5 temperature. After stirring for 16 h the reaction was quenched by the addition of H<sub>2</sub>O, diluted with EtOAc, washed sequentially with 10% aqueous HCl, satd. NaHCO<sub>3</sub>, H<sub>2</sub>O (×3), brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated giving a yellow solid (408 mg). The crude residue was fractionated by flash chromatography (25-100% EtOAc/Hexane) giving *N*-[*N*-((4-dimethylaminophenyl)sulfonyl)-L-leucyl]-L-homophenylalaninamide  
10 (90 mg, 15%) as a white solid. Some title compound (60 mg, 10%) was isolated from this reaction as well.

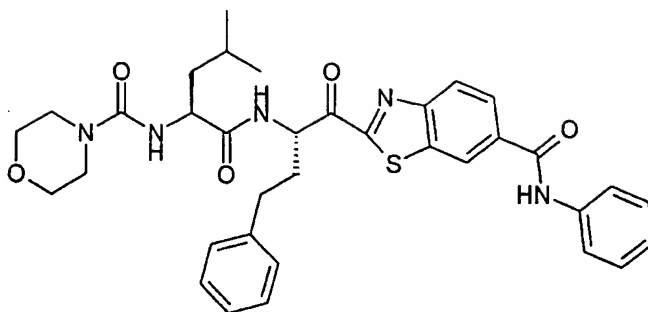
Cyanuric chloride (33 mg, 0.18 mmol) was added to a solution of *N*-[*N*-((4-dimethylaminophenyl)sulfonyl)-L-leucyl]-L-homophenylalaninamide (80 mg, 0.18  
15 mmol) in DMF (2 mL) at 0 °C. After stirring for 2h, the reaction was quenched by addition of satd. NaHCO<sub>3</sub>, filtered, diluted with EtOAc, washed sequentially with H<sub>2</sub>O (×5), brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated giving a yellow foam. The crude residue was fractionated by preparative HPLC (65% AcCN/H<sub>2</sub>O/0.1%TFA) giving the title compound (47 mg, 57%) as a white solid, m.p. 46-48 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ:  
20 7.74(2H, d, *J*= 9), 7.37-7.34 (2H, m), 7.30-7.26 (2H, m), 7.23-7.21 (3H, m), 6.79 (1H, d, *J*=8.5), 4.91 (1H, bs), 4.70 (1H, ddd, *J*=8, 8, 8), 3.68-3.73 (1H,m), 3.06 (3H, s), 2.84-2.76 (2H, m), 2.16-2.09(2H, m), 1.63-1.56 (2H,m), 1.42-1.37 (1H, m), 0.88 (3H, d, *J*=6), 0.71 (3H, d, *J*=6).

25

## EXAMPLE 3.

2-(2-(*S*)-{4-Methyl-2-(*S*)-[(morpholine-4-carbonyl)amino]pentanoylamino}-4-phenylbutyryl)benzothiazole-6-carboxylic acid phenylamide

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As described generally in Method C, N-(t-Boc)-L-homophenylalanine (10.0 g, 35.8 mmol) was dissolved in 50 mL of DMF. The solution was cooled to 0 °C with an ice-water bath. Carbonyldiimidazole (6.4 g, 39.4 mmol) was added to the reaction solution followed by N-methylmorpholine (3.9 g, 39.4 mmol). The reaction was stirred for 1 h at which time N,O-dimethylhydroxylamine hydrochloride (3.8 g, 39.4 mmol) was added. The ice bath was removed and the reaction was stirred at ambient temperature for 3 h. The reaction solution was poured into 200 mL of 1N HCl and extracted with 200 mL of EtOAc. The organic layer was washed with 2 x 100 mL of 1N HCl, 100 mL of saturated sodium bicarbonate, 2 x 100 mL water, and 2 x 100 mL brine. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, decanted and concentrated by rotary evaporation to give the desired amide as a thick oil (11.1 g, 96% crude) which was used without further purification.

The amide (3.7 g, 11.5 mmol), dissolved in 20 mL THF was added dropwise over 20 min to a suspension of LiAlH<sub>4</sub> (0.53 g, 13.9 mmol) in 60 mL THF which was cooled to 0 °C in an ice-water bath. The mixture was stirred for 15 min, then quenched with 10 mL of a saturated solution of sodium bicarbonate, diluted with 200 mL water and extracted with 3x100 mL EtOAc. The organic layers were combined and washed with 100 mL 1 N HCl and 2 x 100 mL brine. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered over a pad of diatomaceous earth and concentrated by rotary evaporation. The residue was purified by flash chromatography (SiO<sub>2</sub>, 5% i-PrOH in CH<sub>2</sub>Cl<sub>2</sub>) to give the desired aldehyde as an oily solid (2.4 g, 79%).

To a dry 100 mL flask was added 6-(phenylcarbamoyl)benzothiazole (0.58 g, 2.3 mmol) and THF (12 mL). The reaction mixture was cooled to  $-78^{\circ}\text{C}$  with a dry-ice/acetone bath. *n*-BuLi (2.5 M in hexanes) (1.8 mL, 4.5 mmol) was added dropwise to the reaction mixture. The reaction was stirred for 20 min to give a suspension. A solution of the  
5 above aldehyde (200 mg, 0.75 mmol) in 3 mL of dry THF was added all at once via syringe. The temperature was gradually increased to  $-40^{\circ}\text{C}$  and the reaction was stirred for 3 h at which time TLC showed consumption of the aldehyde. The reaction was quenched at  $-78^{\circ}\text{C}$  by the addition of a saturated solution of  $\text{NH}_4\text{Cl}$  and the product was extracted with 50 mL EtOAc. The organic layer was dried over  $\text{MgSO}_4$ , filtered and  
10 concentrated to give a residue that was purified by chromatography ( $\text{SiO}_2$ , 2% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to give the desired alcohol as a solid (194 mg, 50%).

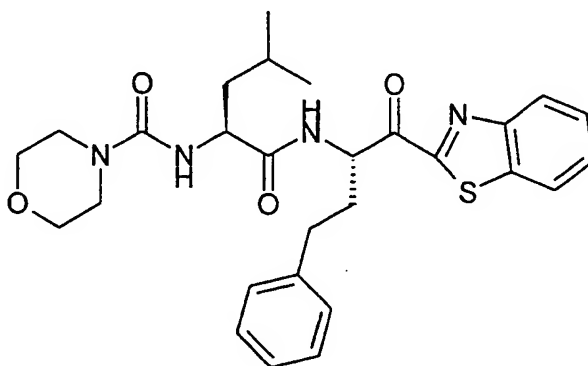
*N*-(4-morpholinecarbonyl)-*L*-leucine (26.4 mg, 0.11 mmol) (prepared as described in Example 1) was dissolved in 2 mL of DMF. The solution was cooled to  $0^{\circ}\text{C}$  with an ice-  
15 water bath and HOBt (19 mg, 0.14 mmol) and EDC (27 mg, 0.14 mmol) were added and the solution stirred for 20 min. The TFA salt of the *N*-deprotected alcohol from above (prepared by stirring the above *N*-Boc protected alcohol in methylene chloride with TFA at room temperature for 30 min and evaporation to dryness) (57 mg, 0.11 mmol  
of *N*-Boc precursor) was added to the reaction as a solution in 1 mL of DMF followed by  
20 addition of *N*-methylmorpholine (35  $\mu\text{L}$ , 0.32 mmol). The reaction was stirred for 3 h, diluted with EtOAc and washed with 10 mL 1N HCl and 10 mL saturated bicarbonate and 2 x 100 mL brine. The organic layer was dried over  $\text{MgSO}_4$ , filtered and concentrated. The residue was purified by chromatography ( $\text{SiO}_2$ , 2% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to give the desired coupled product as a white solid (57 mg, 82%).

25 To the above product (50.4 mg, 0.08 mmol) was added the Dess-Martin periodinane (133 mg, 0.31 mmol), 10 mL  $\text{CH}_2\text{Cl}_2$  and 4 mL *t*-BuOH. The reaction mixture was allowed to stir overnight at room temperature. It was then was diluted with 20 mL  $\text{CH}_2\text{Cl}_2$ , washed with 20 mL of saturated solution of  $\text{Na}_2\text{S}_2\text{O}_3$  and 20 mL  $\text{NaHCO}_3$  solution, the organic  
30 layer was washed with brine, dried over  $\text{MgSO}_4$ , filtered and concentrated. The residue was purified by chromatography ( $\text{SiO}_2$ , 2% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to give the title compound

as a white solid (30 mg, 60%).  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.77-8.70 (1H, m), 8.57-8.52 (1H, m), 8.28-8.20 (1H, m), 8.15-8.07 (1H, m), 7.78-7.68 (2H, m), 7.45-7.35 (2H, m), 7.29-7.05 (7H, m), 5.75-5.65 (1H, m), 5.00-4.92 (1H, m), 4.54-4.41 (1H, m), 3.74-3.58 (4H, m), 3.40-3.24 (4H, m), 2.78-2.62 (2H, m), 2.51-2.32 (1H, m), 2.21-2.02 (1H, m), 1.90-1.40 (3H, m), 1.00-0.80 (6H, m).

## EXAMPLE 4

Morpholine-4-carboxylic acid {1-(S)-[1-(S)-(benzothiazole-2-carbonyl)-3-phenylpropylcarbamoyl]-3-methylbutyl} amide



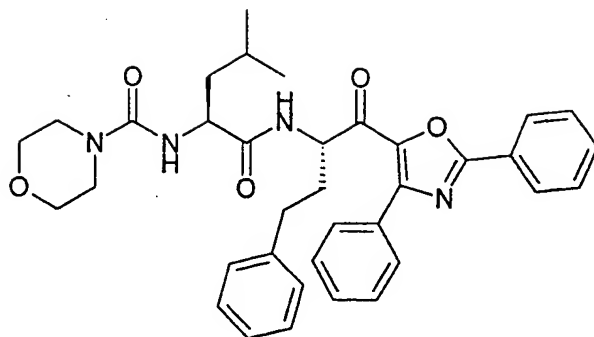
Dry THF (1.5 mL), under Ar, was cooled to  $-78^\circ\text{C}$  with a dry-ice/acetone bath.  $n\text{-BuLi}$  (2.0 M in hexanes) (698  $\mu\text{L}$ , 1.40 mmol) was added to reaction flask followed by dropwise addition of freshly distilled benzothiazole (180 mg, 1.40 mmol) as a solution in 0.5 mL of dry THF. The reaction was stirred for 15 min to give a suspension. A solution of  $N$ -( $t$ -butoxycarbonyl)-( $N'$ -methyl- $N'$ -methoxy)- $L$ -homophenylalaninamide (300 mg, 0.930 mmol) (prepared as described in Example 3) in 1 mL of dry THF was added all at once via syringe. The reaction was stirred for 5 min at which time TLC showed consumption of the amide. The reaction was quenched by the addition of water and the product extracted with 50 mL of EtOAc. The organic layer was dried over  $\text{MgSO}_4$ ,

filtered and concentrated to give a residue that was purified by preparative TLC (CH<sub>2</sub>Cl<sub>2</sub>) to give the desired ketone as a clear colorless oil.

*N*-(4-morpholinecarbonyl)-L-leucine (82 mg, 0.34 mmol) (prepared as described in Example 1) was dissolved in 2 mL of DMF. The solution was cooled to 0 °C with an ice-water bath and HOBt (60 mg, 0.44 mmol) and EDC (83 mg, 0.44 mmol) were added and the solution stirred for 20 min. The TFA salt of the *N*-deprotected ketone from above (prepared by stirring the above *N*-Boc protected alcohol in methylene chloride with TFA at room temperature for 30 min and evaporation to dryness) (133 mg, 0.34 mmol of *N*-Boc precursor) was added to the reaction as a solution in 1 mL of DMF followed by addition of *N*-methylmorpholine (77 µL, 0.70 mmol). The reaction was stirred for 3 h, diluted with EtOAc and washed with 100 mL 1N HCl and 100 mL saturated bicarbonate and 2 x 100 mL brine. The organic layer was dried over MgSO<sub>4</sub>, filtered and concentrated. The residue was purified by chromatography (SiO<sub>2</sub>, 50% EtOAc in hexane) to give the title compound as a white solid (40 mg, 23%) that was shown to be a 1 to 1 mixture of two epimers. <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>): δ 8.15-8.08 (1H, m), 7.98-7.88 (1H, m), 7.60-7.40 (2H, m), 7.25-7.07 (5H, m), 7.02-6.92 (1H, m), 5.90-5.75 (1H, m), 4.98-4.90 (1H, m), 4.50-4.35 (1H, m), 3.66-3.57 (4H, m), 3.40-3.30 (4H, m), 2.80-2.70 (2H, m), 2.50-2.35 (1H, m), 2.25-2.10 (1H, m), 1.80-1.40 (3H, m), 1.00-0.88 (6H, m).

#### EXAMPLE 5

**Morpholine-4-carboxylic acid {1-(*S*)-[1-(*S*)-(2,4-diphenyloxazole-5-carbonyl)-3-phenylpropylcarbamoyl]-3-methylbutyl} amide**



- As outlined generally in Scheme IV (Method D), 2,4-diphenyloxazole (361 mg, 1.63 mmol) in 15 mL dry THF was cooled to -78 °C and *n*-butyllithium (1.16 mL of a 1.4 M solution, 1.63 mmol) was added. After stirring for 1 h at -78 °C, a solution of the free base of *N*-[*N*-(*t*-butoxycarbonyl)-L-leuciny]-L-homophenylalaninamide (prepared as described in Example 3) in 5 mL of dry THF was added dropwise. The temperature of the reaction mixture was allowed to rise to -20 °C and maintained for 2 h after which time the reaction mixture was quenched with 100 mL of NH<sub>4</sub>Cl (10% aqueous) and extracted with 3 x 100 mL EtOAc. The combined extracts were washed with 2 x 100 mL brine, dried with Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated. The resulting residue was purified by chromatography (florisil, 15% - 20% hexane in EtOAc) yielding 190 mg (72%) of [1-(2,4-diphenyloxazole-5-carbonyl)-3-phenylpropyl]carbamic acid tert-butyl ester.
- N*-[(4-Morpholinyl)carbonyl]-L-leucine (100 mg, 0.35 mmol) (prepared as described in Example 1) was dissolved in 10 mL DMF and cooled to 0 °C. To the solution was added EDC (77 mg, 0.4 mmol) and HOBt (54 mg, 0.4 mmol) and the reaction was stirred for 1h. In a separate flask, [1-(2,4-diphenyloxazole-5-carbonyl)-3-phenylpropyl]carbamic acid tert-butyl ester (158 mg, 0.31 mmol) was dissolved in 4 mL CH<sub>2</sub>Cl<sub>2</sub> and 2 mL TFA was added. After stirring for 1 h, the solvents were evaporated, the residue was dissolved in 5 mL DMF and *N*-methylmorpholine (406 mg, 0.4 mmol) was added. The resulting solution was added to the previously prepared solution of activated leucine derivative at 0 °C. The reaction mixture was stirred at room temperature for 3 h, cooled to 0 °C, and quenched with 100 mL of a 10% solution of citric acid in water. The resulting mixture was extracted with 3 x 100 mL EtOAc. The combined organic extracts were washed with



2 x 100 mL of saturated bicarbonate and 1 x 100 mL brine. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to a residue that was purified by chromatography (florisil, 30% - 50% EtOAc in hexane) to give the title compound as a white solid (90mg, 84%), m.p. 83-5 °C, MS (ES) 609 (M<sup>+</sup>).

5

The following compounds were also prepared using the procedure described in Example 5:

10 Morpholine-4-carboxylic acid {1-(*S*)-[1(*S*)-(2,4-diphenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethylbutyl} amide, m.p. 95-7 °C, MS (ES) 623 (M<sup>+</sup>).

15

Morpholine-4-carboxylic acid {2-cyclohexyl-1-(*S*)-[1-(*S*)-(2,4-diphenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl} amide, m.p. 93-5 °C, MS (ES) 649 (M<sup>+</sup>).

Morpholine-4-carboxylic acid {1-(*S*)-[2,4-diphenyl-oxazole-5-yl]-2-oxo-ethylcarbamoyl]-3-methylbutyl} amide, m.p. 155-7 °C, MS (ES) 505 (M<sup>+</sup>).

20

Morpholine-4-carboxylic acid {2-cyclohexyl-1-(*S*)-[2-(2,4-diphenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl}-amide, m.p. 122-3 °C, MS (ES) 545 (M<sup>+</sup>).

Morpholine-4-carboxylic acid {1-(*S*)-[2-(2,4-diphenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3,3-dimethylbutyl}-amide, m.p. 97-9 °C, MS (ES) 519 (M<sup>+</sup>).

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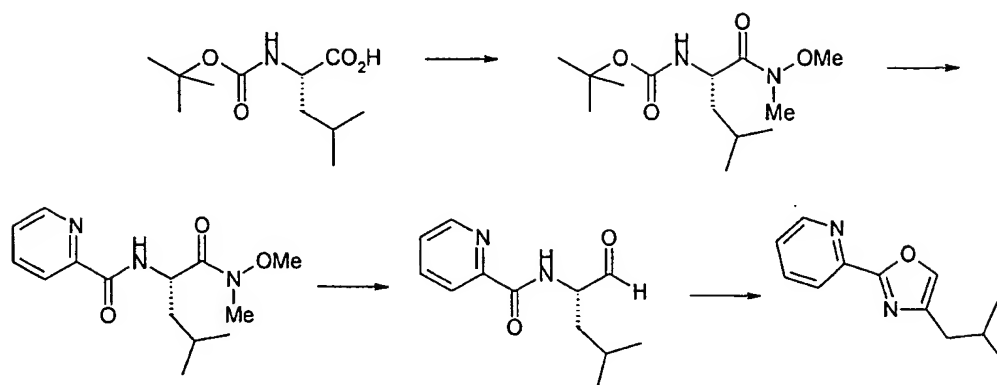
Morpholine-4-carboxylic acid (1-(*S*)-{1-(*S*)-[2-(3-benzyloxy-phenyl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide, m.p. 61-3 °C, MS (ES) 639 (M<sup>+</sup>).

30

Morpholine-4-carboxylic acid {2-cyclohexyl-1-(*S*)-[1-(*R,S*)-(4-isobutyl-2-pyrimidin-2-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl]-ethyl} amide, m.p. 93-5 °C, MS (ES) 649 (M<sup>+</sup>).

## EXAMPLE 6

## 5 2-(4-Isobutyloxazol-2-yl)pyridine (Method E)



- 10 *N*-(*t*-Butoxy)-L-leucine (10 g, 43 mmol) was dissolved in 200 mL of CH<sub>2</sub>Cl<sub>2</sub>. The solution was cooled to 0 °C with an ice-water bath. Carbonyldiimidazole (7.7 g, 47.5 mmol) was added and the reaction mixture was stirred for 1 h. *N,O*-dimethylhydroxylamine hydrochloride (4.64 g, 47.8 mmol) was added at 0 °C. The ice bath was removed and the reaction was stirred at ambient temperature for 16 h.
- 15 The reaction solution was poured into 200 mL of an ice-cooled solution of 5% citric acid. The organic layer was separated, washed with 2 x 100 mL of 1N HCl, 1 x 100 mL of saturated NaHCO<sub>3</sub>, and 2 x 100 mL brine. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated by rotary evaporation to give [1-(*N*-methoxy-*N*-methylcarbamoyl)-3-methylbutyl]carbamic acid tert-butyl ester as a thick oil (7.39 g,
- 20 59% crude) which was used without further purification.

The tert-butyl ester from above (1g, 3.47 mmol) was dissolved in 10 mL CH<sub>2</sub>Cl<sub>2</sub> and 5 mL trifluoroacetic acid was added. The reaction mixture was stirred for 1 h. Solvents were evaporated and the residue was taken up in 2 x 10 mL CH<sub>2</sub>Cl<sub>2</sub> and evaporated to an

oil. In a separate flask, picolinic acid (470 mg, 3.82 mmol) was dissolved in 10 mL DMF and the resulting solution was cooled to 0 °C. EDC (787 mg, 4.1 mmol) and HOBT (554 mg, 4.1 mmol) were added and the reaction mixture was stirred at 0 °C for 1 h. In a separate flask, the free amine prepared above was dissolved in 5 mL DMF and 1.5 mL N-methylmorpholine was added. This solution was added to the reaction mixture at 0 °C. The reaction mixture was allowed to stir at ambient temperature for 16 h after which time it was poured into a mixture of ice/5% citric acid (100 mL) and extracted with 4 x 30 mL EtOAc. The combined EtOAc extracts were washed with 3 x 100 mL brine, 2 x 100 mL NaHCO<sub>3</sub>, 1 x 100 mL brine, dried with Na<sub>2</sub>SO<sub>4</sub>, and evaporated to an oil which was dried under vacuum yielding 990 mg (100%) of pyridine-2-carboxylic acid [1-(N-methoxy-N-methylcarbamoyl)-3-methylbutyl]amide. This was used without further purification.

The amide from above (4.7 g, 14.7 mmol) was dissolved in 50 mL THF and added to a slurry of LiAlH<sub>4</sub> (558 mg, 14.7 mmol) in 50 mL THF at -78 °C. The reaction mixture was allowed to warm to 0 °C and maintained for 15 min, after which time it was cooled to -78 °C and cannulated into an ice-cooled solution of KHSO<sub>4</sub> (8.16 g, 60 mmol) in 200 mL H<sub>2</sub>O. The resulting mixture was extracted with 5 x 100 mL EtOAc. The combined extracts were washed with 2 x 100 mL satd. NaHCO<sub>3</sub> and 1 x 100 mL brine, dried with Na<sub>2</sub>SO<sub>4</sub> and evaporated to an oily residue which was flash chromatographed through SiO<sub>2</sub> (25% EtOAc/hexane – 35% EtOAc/hexane) yielding 2.8 g (86%) of pyridine-2-carboxylic acid (1-formyl-3-methylbutyl)amide as a colorless oil which solidified on standing.

Hexachloroethane (445 mg, 1.87 mmol) was dissolved in 5 mL CH<sub>3</sub>CN. A solution of pyridine-2-carboxylic acid (1-formyl-3-methylbutyl)amide (137.5 mg, 0.625 mmol) in 2 mL CH<sub>3</sub>CN was added followed by triethylamine (375 mg, 3.75 mmol) and triphenylphosphine (491 mg, 1.87 mmol). The resulting mixture was stirred for ½ h, poured into brine, and extracted with 2 x 25 mL EtOAc. The combined extracts were washed with 1 x 50 mL brine, dried with Na<sub>2</sub>SO<sub>4</sub> and evaporated to 665 mg of a tan solid which was flash chromatographed through SiO<sub>2</sub> (20% - 35% hexane/EtOAc) yielding 100 mg (76%) of the title compound as an amber oil, MS (ES) 203 (M<sup>+</sup>).

## ASSESSMENT OF BIOLOGICAL PROPERTIES

5

### Expression and Purification of recombinant human Cathepsin S

Cloning of human cathepsin S:

U937 RNA was subjected to reverse transcriptase / polymerase chain reaction with  
10 primer A (5'cacaatgaaacggctgggttg 3') and primer B (5'ctagattctgggtaagaggg 3')  
designed to specifically amplify the cathepsin S cDNA. The resulting 900 bp DNA  
fragment was subcloned into pGEM-T (Promega) and sequenced to confirm its identity.  
This construct was used for all subsequent manipulations. This procedure is typical for  
cloning of known genes and is established in its field.

15

Human Pre-Pro-Cat S was removed from pGem-T vector (Promega, 2800 Woods Hollow  
Rd, Madison, WI 53711) by digestion with restriction enzyme SacII, followed by  
treatment with T4 DNA polymerase to generate a blunt end, and a second restriction  
enzyme digest with SalI. It was subcloned into pFastBac1 donor plasmid (GibcoBRL,  
20 8717 Grovemont Cr., Gaithersburg, MD 20884) which had been cut with restriction  
enzyme BamHI and blunt-ended and then cut with restriction enzyme SalI. The ligation  
mixture was used to transform DH5a competent cells (GibcoBRL) and plated on LB  
plates containing 100ug/ml ampicillin. Colonies were grown in overnight cultures of LB  
media containing 50ug/ml Ampicillin, plasmid DNA isolated and correct insert  
25 confirmed by restriction enzyme digestion. Recombinant pFastBac donor plasmid was  
transformed into DH10Bac competent cells (GibcoBRL). Large white colonies were  
picked from LB plates containing 50ug/ml kanamycin, 7ug/ml gentamicin, 10ug/ml  
tetracycline, 100ug/ml Blueo-gal, and 40ug/ml IPTG. DNA was isolated and used to  
transfect Sf9 insect cells using CellFECTIN reagent (GibcoBRL). Cells and supernatant  
30 were harvested after 72 hours. Viral supernatant was passaged twice and presence of Cat  
S confirmed by PCR of the supernatant.

SF9 cells were infected with recombinant baculovirus at a MOI of 5 for 48-72 hrs. Cell pellet was lysed and incubated in buffer at pH 4.5 at 37 for 2 hours to activate Cat S from pro-form to active mature form (Bromme, D & McGrath, M., Protein Science, 1996, 5:789-791.) Presence of Cat S was confirmed by SDS-PAGE and Western blot using  
5 rabbit anti-human proCat S.

#### Inhibition of Cathepsin S

Human recombinant cathepsin S expressed in Baculovirus is used at a final concentration  
10 of 10nM in buffer. Buffer is 50mM Na Acetate, pH 6.5, 2.5mMEDTA, 2.5mMTCEP. Enzyme is incubated with either compound or DMSO for 10 min at 37C. Substrate 7-amino-4-methylcoumarin, CBZ-L-valyl-L-valyl-L-arginineamide (custom synthesis by Molecular Probes) is diluted to 20uM in water (final concentration of 5uM), added to assay and incubated for additional 10 minutes at 37 C. Compound activity is measured  
15 by diminished fluorescence compared to DMSO control when read at 360nm excitation and 460nm emission.

Examples listed above were evaluated for inhibition of cathepsin S in the above assay. All had IC<sub>50</sub> of 100 micromolar or below.

20

The following prophetic compounds may be made in accordance with the procedure outlined in Scheme IV (Method D), and the specific example 5:

25 Morpholine-4-carboxylic acid {1-[2-(4-isobutyl-2-pyridin-2-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;

Morpholine-4-carboxylic acid {1-[2-(4-cyclohexylmethyl-2-pyridin-2-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;

30 Morpholine-4-carboxylic acid {1-[2-(4-cyclohexylmethyl-2-pyridin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;

Morpholine-4-carboxylic acid {2-cyclohexyl-1-[2-(4-cyclohexylmethyl-2-pyridin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl}-amide;

35

- Morpholine-4-carboxylic acid {2-cyclohexyl-1-[2-(4-isobutyl-2-pyridin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl}-amide;
- 5 Morpholine-4-carboxylic acid {1-[2-(4-isobutyl-2-pyridin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;
- Morpholine-4-carboxylic acid {1-[1-(4-isobutyl-2-pyridin-3-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3-methyl-butyl}-amide;
- 10 Morpholine-4-carboxylic acid {1-[1-(4-isobutyl-2-pyridin-3-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethyl-butyl}-amide;
- Morpholine-4-carboxylic acid {1-[1-(4-isobutyl-2-pyridin-4-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethyl-butyl}-amide;
- 15 Morpholine-4-carboxylic acid {2-cyclohexyl-1-[1-(4-isobutyl-2-pyridin-4-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl}-amide;
- Morpholine-4-carboxylic acid {2-cyclohexyl-1-[1-(4-cyclohexylmethyl-2-pyridin-4-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl}-amide;
- 20 Morpholine-4-carboxylic acid (2-cyclohexyl-1-{1-[4-isobutyl-2-(1-methylpiperidin-4-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-ethyl)-amide;
- 25 Morpholine-4-carboxylic acid (1-{1-[4-isobutyl-2-(1-methyl-piperidin-4-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- Morpholine-4-carboxylic acid (1-{1-[4-isobutyl-2-(1-pyrimidin-2-yl-piperidin-4-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- 30 Morpholine-4-carboxylic acid (1-{2-[4-isobutyl-2-(1-pyrimidin-2-yl-piperidin-4-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- Morpholine-4-carboxylic acid (1-{2-[4-cyclohexylmethyl-2-(1-pyrimidin-2-yl-piperidin-4-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3-methyl-butyl)-amide;
- 35 Morpholine-4-carboxylic acid {1-[2-(4-cyclohexylmethyl-2-piperidin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;
- 40 Morpholine-4-carboxylic acid {1-[2-(4-isobutyl-2-piperidin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;
- Morpholine-4-carboxylic acid (1-{2-[4-isobutyl-2-(1-methyl-piperidin-3-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3-methyl-butyl)-amide;
- 45

- Morpholine-4-carboxylic acid (1-{2-[4-isobutyl-2-(1-methyl-piperidin-3-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- 5 Morpholine-4-carboxylic acid (1-{2-[4-isobutyl-2-(1-methyl-piperidin-2-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- Morpholine-4-carboxylic acid (1-{1-[4-isobutyl-2-(1-methyl-piperidin-2-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide;
- 10 Morpholine-4-carboxylic acid {1-[4-isobutyl-2-phenyl-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide;
- Morpholine-4-carboxylic acid {1-[1-(4-dimethylaminomethyl-2-phenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3-methyl-butyl)-amide;
- 15 Morpholine-4-carboxylic acid {1-[2-(4-dimethylaminomethyl-2-phenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl)-amide;
- Morpholine-4-carboxylic acid {2-cyclohexyl-1-[2-(4-dimethylaminomethyl-2-phenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl)-amide;
- 20 Morpholine-4-carboxylic acid {1-[2-(4-dimethylaminomethyl-2-phenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3,3-dimethyl-butyl)-amide;
- 25 Morpholine-4-carboxylic acid {1-[1-(4-dimethylaminomethyl-2-phenyl-oxazol-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethyl-butyl)-amide;
- Morpholine-4-carboxylic acid {1-[1-(4-hydroxymethyl-2-phenyl-oxazol-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethyl-butyl)-amide;
- 30 Morpholine-4-carboxylic acid (3,3-dimethyl-1-{2-[4-(4-methyl-piperazin-1-ylmethyl)-2-phenyl-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-butyl)-amide;
- Morpholine-4-carboxylic acid (3,3-dimethyl-1-{2-[4-(4-methyl-piperazin-1-ylmethyl)-2-pyridin-4-yl-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-butyl)-amide;
- 35 Morpholine-4-carboxylic acid (3-methyl-1-{1-[4-(4-methyl-piperazin-1-ylmethyl)-2-pyridin-4-yl-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-butyl)-amide;
- 40 {1-[4-Isobutyl-5-(2-{4-methyl-2-[(morpholine-4-carbonyl)-amino]-pentoylamino}-acetyl)-oxazol-2-yl]-3-methyl-butyl}carbamic acid benzyl ester;
- Morpholine-4-carboxylic acid {2-cyclohexyl-1-[1-(4-isobutyl-2-pyrimidin-4-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl)-amide;
- 45

Morpholine-4-carboxylic acid {2-cyclohexyl-1-[3-phenyl-1-(4-phenyl-2-pyridin-4-yl-thiazole-5-carbonyl)-propylcarbamoyl]-ethyl}-amide; and

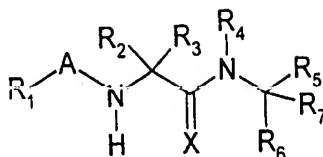
- 5 Morpholine-4-carboxylic acid {2-cyclohexyl-1-[2-oxo-2-(2-pyridin-4-yl-4-*p*-tolyl-thiazole-5-yl)-ethylcarbamoyl]-ethyl}-amide.

Preferred prophetic compounds have S-stereochemistry at their asymmetric carbons.



# What is claimed is:

1. A compound of formula (I):



(I)

wherein:

A is -C(Y)- or -SO<sub>2</sub>-

Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

R<sub>1</sub> is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycle, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>2</sub> is H or alkyl;

R<sub>3</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>3</sub> is optionally substituted by one or more groups of the formula R<sub>d</sub>;

5

R<sub>d</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

20

R<sub>e</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25

R<sub>4</sub> is H or alkyl;

R<sub>5</sub> is H, alkyl or cycloalkyl;

30

R<sub>6</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>6</sub> is optionally substituted by one or more groups of the formula R<sub>f</sub>;

35

R<sub>f</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, heteroarylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono

40

45

or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

5  $R_g$  is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by halogen, C1-5alkyl or C1-5alkoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or  
10 heteroaryl; alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or  
15 heteroaryl; alkoxycarbonylamino, aryloxy, carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

20 or  $R_5$  together with  $R_6$  form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more  $R_h$ ;

25  $R_h$  is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxy, carbonyl, arylalkoxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl or heteroaryl; halogen, hydroxy, carboxy and cyano;

30  $R_7$  is  $R_8-C(Z)-$ ;

wherein Z is O, S, or  $NR_i$  wherein  $R_i$  is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy and hydroxy;

35  $R_8$  is a 5-8 membered monocyclic heteroaryl or 8-11 membered bicyclic heteroaryl ring system, each of the monocyclic or bicyclic ring systems having 1-4 of the same or different heteroatoms selected from the group consisting of N, O and S wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

40  $R_j$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, alkoxycarbonyl, aryloxy, carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur  
45 atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen

atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxycarbonylamino, aryloxy carbonylamino, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy carbonylamino, arylalkoxy carbonylamino, arylalkoxy carbonylaminoalkyl, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

X is O, S or N-OH;

and the pharmacutrically acceptable derivatives thereof;

with the proviso that when  $R_6$  is alkyl the alkyl must be substituted with  $R_f$  wherein  $R_f$  is not hydroxy, sulfhydryl or halogen.

2. The compound according to claim 1 wherein:

$R_a$  is selected from the group consisting of H, alkyl and aryl;

$R_1$  is C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranal, thiopyranal, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

5 R<sub>b</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

45 R<sub>c</sub> is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;

heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>3</sub> is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

R<sub>d</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,

5 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_d$  may be further optionally substituted by one or more  $R_c$ ;

10  $R_c$  is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

15  $R_s$  is H or alkyl;

$R_6$  is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

20  $R_f$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, 25 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxy carbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl 30 wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, 35 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either 40 nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, 45

pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy-carbonylamino, aryloxy-carbonylamino, C1-8 alkylcarbamoxyloxy, 5 arylcarbamoxyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, 10 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, 15 cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, C1-3alkyl or C1-3alkoxy; 20 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, 25 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxy-carbonyl, aryloxy-carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the 30 nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, 35 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom 40 may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl 45 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,



5       tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,  
       indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
       benzthiazolyl, benzoxazolyl, purinyl, quinoliny, isoquinoliny,  
       quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl or phenoxazinyl,  
 10       alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy,  
       arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,  
       alkylaminosulfonyl and arylaminosulfonyl, amino wherein the nitrogen  
       atom may be independently mono or di-substituted by alkyl, aryl,  
 15       heterocyclyl selected from the group consisting of pyrrolidinyl,  
       piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or  
       heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
       oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,  
       triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
       pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 20       benzthiazolyl, benzoxazolyl, purinyl, quinoliny, isoquinoliny,  
       quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl,  
       halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

20       R<sub>b</sub> is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxycarbonyl,  
       aryloxycarbonyl, arylC1-8alkoxycarbonyl, carbamoyl wherein the nitrogen atom  
       may be optionally mono or di-substituted with a group selected from C1-8 alkyl,  
       C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group  
 25       consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl  
       and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,  
       pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,  
       triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,  
       indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
 30       benzoxazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny,  
       carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, carboxy and  
       cyano;

35       R<sub>8</sub> is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl,  
       oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl,  
       pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl,  
       benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, triazolyl,  
       tetrazolyl, purinyl, quinoliziny, quinoliny, isoquinoliny, cinnoliny, phthalazinyl,  
 40       quinazoliny, quinoxaliny, naphthyridiny, pteridiny, carbazolyl, acridiny and  
       phenazinyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

45       R<sub>j</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl  
       selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,  
       thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group  
       consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl,

isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, 5 arylalkyl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of 10 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, 15 aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, 20 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, 25 quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxy carbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, 30 piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazoliny, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, 35 oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

40 R<sub>k</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, 45 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,

5 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,  
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl,  
alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be  
independently mono or di-substituted by alkyl, aryl, heterocyclyl selected  
10 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,  
thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the  
group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,  
imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,  
thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,  
isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,  
quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
15 alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be  
oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be  
oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom  
may be independently substituted by alkyl, aryl, heterocyclyl selected  
from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,  
thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the  
20 group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,  
imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,  
thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,  
isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,  
25 quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
alkoxycarbonylamino, aryloxycarbonylamino, arylalkoxycarbonylamino,  
arylalkoxycarbonylaminoalkyl, C1-8 alkylcarbamoyloxy,  
arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,  
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom  
30 may be independently mono or di-substituted by alkyl, aryl, heterocyclyl  
selected from the group consisting of pyrrolidinyl, piperidinyl,  
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl  
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,  
35 tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,  
indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,  
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

40 and X is O or S.

45 3. The compound according to claim 2 wherein:

Y is O or S;

- 5 R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranly, thiopyranly, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

- 15 R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
20 wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro,



imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_4$  is H or C1-3 alkyl;

$R_5$  is H or C1-8 alkyl;

$R_6$  is H, C1-5 alkyl, C3-7 cycloalkyl or aryl wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,

quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5  
 alkoxycarbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be  
 5 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected  
 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,  
 thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group  
 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl,  
 tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
 10 benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl,  
 quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro,  
 amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  
 $R_g$ ;

15  $R_g$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl,  
 aryl optionally substituted by halogen, methyl or methoxy; heterocyclyl  
 selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 20 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,  
 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and  
 quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5  
 alkoxycarbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
 25 wherein the nitrogen atom may be independently mono or di-substituted  
 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of  
 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and  
 indolinyl or heteroaryl selected from the group consisting of furanyl,  
 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,  
 30 pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl,  
 quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5  
 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or  
 sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or  
 35 sulfone, ureido wherein either nitrogen atom may be independently  
 substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group  
 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,  
 piperazinyl and indolinyl, or heteroaryl selected from the group consisting  
 of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl,  
 40 tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl,  
 isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino,  
 aryloxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5  
 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,  
 45 arylaminosulfonyl, amino wherein the nitrogen atom may be  
 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl

selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_h$  is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, carboxy and cyano;

$R_i$  is alkoxy, aryloxy or hydroxy;

$R_8$  is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliziny, quinolinyl, isoquinolinyl, cinnoliny, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

$R_j$  is selected from the group consisting of C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl; arylC1-8alkyl, C1-8alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl



5 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either  
 10 nitrogen atom may be independently substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group  
 20 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_j$  may be further optionally substituted by  
 25 one or more  $R_k$ ;

35  $R_k$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or  
 40 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,

oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkoxycarbonylamino, aryloxycarbonylamino, arylC1-8alkoxycarbonylamino, arylalkoxycarbonylamino, C1-8alkyl, C1-8alkylcarbamoyloxy, arylcarbamoyloxy, C1-8alkylsulfonylamino, arylsulfonylamino, C1-8alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino.

4. The compound according to claim 3 wherein:

Y is O;

R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

5  $R_b$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or  
10 di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio  
15 wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
20 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of  
25 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

30  $R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, and cyano;

$R_2$  is H or methyl;

35  $R_3$  is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

40  $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen  
45 atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of

furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,  
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,  
 quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio  
 wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio  
 wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein  
 either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl,  
 naphthyl, heterocyclyl selected from the group consisting of piperidinyl,  
 morpholinyl and piperazinyl or heteroaryl selected the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,  
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,  
 quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxy carbonylamino,  
 C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,  
 arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein  
 the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl,  
 phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl,  
 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,  
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,  
 quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may  
 be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,  
 aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino,  
 halogen, hydroxy, oxo, carboxy and cyano;

R<sub>4</sub> is H or methyl;

R<sub>5</sub> is H or C1-5 alkyl;

R<sub>6</sub> is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl or naphthyl wherein R<sub>6</sub> is optionally  
 substituted by one or more R<sub>f</sub>;

R<sub>f</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,  
 naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,  
 quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy,  
 arylC1-5alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5  
 alkoxycarbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
 wherein the nitrogen atom may be independently mono or di-substituted by C1-5

alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; naphthyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and

5 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl  
 10 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;

20  $R_h$  is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano;

30 Z is O or S;

35  $R_g$  is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliziny, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxaliny, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above  $R_g$  can be optionally substituted by one or more groups of the formula  $R_j$ ;

40  $R_j$  is selected from the group consisting of C1-5alkyl, C3-6cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, arylC1-5alkyl, C1-5alkoxy, aryloxy, arylC1-

5alkoxy, C1-5alkoxycarbonyl, aryloxycarbonyl, C1-5alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkanoylamino, aroylamino, C1-5alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5alkylsulfonylamino, arylsulfonylamino, C1-5alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, Rj may be further optionally substituted by one or more R<sub>k</sub>;

R<sub>k</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, tetrazolyl and pyridinyl, C1-3 alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, aryl, heterocyclyl selected from the group consisting of morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, and pyridinyl, C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl, phenyl, naphthyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-3alkoxycarbonylamino, aryloxycarbonylamino, arylC1-3alkoxycarbonylamino, benzyloxycarbonylamino, C1-5alkyl, C1-3alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino,

arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro;

and

X is O.

5.

The compound according to claim 4 wherein:

R<sub>1</sub> is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranal and thiopyranal; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub>

is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxycarbonyl, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aryloxy, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,



thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

5

$R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

$R_2$  is H;

10

$R_3$  is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

15

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkoxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkyl sulfonylamino, aryl sulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

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$R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, aryl C1-3 alkyl, C1-5 alkoxy, phenoxy, aryl C1-3 alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

wherein the configuration at the stereocenter defined by  $R_2$  and  $R_3$  and the carbon they are attached to is L;

45

R<sub>4</sub> is H;

R<sub>5</sub> is H or C1-3 alkyl;

R<sub>6</sub> is H, C1-5 alkyl, C3-6 cycloalkyl or phenyl. wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

10 R<sub>f</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group  
 15 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or  
 20 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
 25 independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
 30 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

35 R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy,  
 40 arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom  
 45 may be independently substituted by C1-5 alkyl or aryl; C1-5

alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom  
 may be independently mono or di-substituted by C1-5 alkyl or aryl;  
 5 halogen, hydroxy, oxo, carboxy and cyano;

R<sub>h</sub> is selected from the group consisting of C1-5 alkyl, phenyl, C1-5  
 10 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein  
 the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-  
 6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, halogen, hydroxy, carboxy and  
 cyano;

15 wherein Z is O;

R<sub>g</sub> is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl,  
 imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl,  
 20 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
 benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, wherein any of  
 the above R<sub>g</sub> can be optionally substituted by one or more R<sub>j</sub>;

R<sub>j</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl,  
 25 naphthyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl,  
 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,  
 arylC1-3alkyl, C1-3alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl,  
 aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen  
 atom may be independently mono or di-substituted by C1-3alkyl, phenyl,  
 30 naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
 tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; C1-3alkanoylamino,  
 aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide  
 or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or  
 35 sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide  
 or sulfone, ureido wherein either nitrogen atom may be independently substituted  
 by C1-3 alkyl, phenyl, naphthyl, piperidinyl, morpholinyl, thiazolyl, imidazolyl,  
 tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; C1-3  
 40 alkoxycarbonylamino, aryloxycarbonylamino, C1-3 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-  
 3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may  
 be independently mono or di-substituted by C1-3 alkyl, phenyl, naphthyl,  
 piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl,  
 45 pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,

benzoxazolyl, quinolinyl or isoquinolinyl; halogen, hydroxy, oxo, carboxy, cyano and nitro,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, morpholinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; arylC1-3alkoxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, naphthyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro.

6. The compound according to claim 5 wherein:

$R_1$  is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl; C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl,

heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

$R_3$  is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxy, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_6$  is H, C1-5 alkyl or phenyl wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridyl, C1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

5  $R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

20  $R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, phenyl, benzyl, halogen, hydroxy, carboxy and cyano;

25  $R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

30  $R_j$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, benzyl, C1-3alkoxy, phenoxy, benzyloxy, C1-3alkoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, thiazolyl, imidazolyl or pyridinyl; C1-3 alkoxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; halogen, hydroxy, carboxy, cyano and nitro,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

45

5  $R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, pyridinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; acetylamino, benzoylamino, methylthio  
10 wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl and thiazolyl, benzyloxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl, halogen, hydroxy, carboxy, cyano and nitro.

15

7. The compound according to claim 6 wherein:

20

$R_1$  is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyranal, thiopyranal or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

25

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido  
30 wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

35

$R_c$  is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

40

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3alkoxy, C1-5alkoxycarbonyl, C1-5alkanoyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl; C1-5alkanoylamino, C1-3 alkylthio wherein the sulfur atom  
45 may be oxidized to a sulfoxide or sulfone, C1-3alkoxycarbonylamino, C1-3alkylsulfonylamino, amino wherein the nitrogen atom may be independently

mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

5  $R_e$  is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_5$  is H or methyl;

10  $R_6$  is C1-5 alkyl or phenyl, wherein  $R_6$  is optionally substituted by one or more groups of the formula  $R_f$ ,

15  $R_f$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy-carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5  
20 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen or methyl; C1-3 alkoxy, aryloxy, benzyloxy, C1-3  
25 alkoxy-carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

30

$R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy-carbonyl, benzyloxy and carboxy;

35

$R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzimidazolyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

40  $R_j$  is selected from the group consisting of methyl, cyclohexyl, phenyl, furanyl, thienyl, benzyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; acetylamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl  
45 or phenyl; methoxycarbonylamino, C1-3 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by



methyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy and cyano,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

5  $R_k$  is selected from the group consisting of methyl, phenyl, furanyl, thienyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently  
10 mono or di-substituted by methyl or phenyl; acetamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylaminoC1-3alkyl, amino wherein the nitrogen atom may be independently mono or  
15 di-substituted by C1-3alkyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy, cyano and nitro.

8. The compound according to claim 7 wherein:

20 A is -C(O)- or -SO<sub>2</sub>-;

$R_1$  is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranlyl, thiopyranlyl or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

25  $R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-  
30 substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

35  $R_c$  is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy;

$R_3$  is C1-5 alkyl or C5-6 cycloalkyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

40  $R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally  
45 substituted by one or more  $R_e$ ;

R<sub>e</sub> is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

5 R<sub>f</sub> is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently  
10 mono or di-substituted by C1-3 alkyl; halogen, hydroxy, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of methyl, phenyl optionally substituted by halogen or methyl; methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently  
15 mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy and carboxy;

20 R<sub>h</sub> is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R<sub>h</sub> can be optionally substituted by one or more R<sub>j</sub>;

25 R<sub>j</sub> is selected from the group consisting of methyl, phenyl, furanyl, thienyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetylamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by  
30 methyl or phenyl; halogen, hydroxy, carboxy and cyano, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

35 R<sub>k</sub> is selected from the group consisting of methyl, phenyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy, cyano and nitro.  
40

9. The compound according to claim 8 wherein:

45

R<sub>1</sub> is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

5 R<sub>b</sub> is selected from the group consisting of, pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy and carboxy, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

10 R<sub>c</sub> is selected from the group consisting of methoxy, halogen and hydroxy;

15 R<sub>d</sub> is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

20 R<sub>5</sub> is H;

25 R<sub>f</sub> is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

30 R<sub>g</sub> is selected from the group consisting of methyl, phenyl optionally substituted by halogen; methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

35 R<sub>8</sub> is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

40 R<sub>j</sub> is selected from the group consisting of methyl, phenyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; methoxycarbonylamino, halogen, hydroxy and carboxy, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

45 R<sub>k</sub> is selected from the group consisting of methyl, phenyl, methoxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; benzyloxycarbonylamino, amino wherein the nitrogen atom may be

independently mono or di-substituted by methyl or phenyl; halogen, hydroxy and carboxy.

5

10. The compound according to claim 9 wherein:

10  $R_1$  is phenyl or 4-morpholinyl, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino,  $R_b$  may be further optionally substituted by a halogen atom;

15  $R_3$  is C1-5 alkyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C3-6 cycloalkyl and phenyl,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

20  $R_e$  is selected from the group consisting of methyl and halogen;

$R_6$  is C1-5 alkyl optionally substituted by one or more  $R_f$ ;

25  $R_f$  is selected from the group consisting of C5-6 cycloalkyl, phenyl, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, and halogen,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy;

30

$R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

35

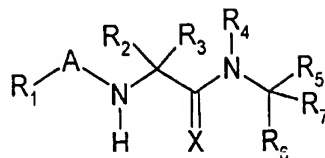
$R_j$  is selected from the group consisting of phenyl, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or disubstituted by methyl or phenyl; methoxycarbonylamino and halogen,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

40

$R_k$  is selected from the group consisting of phenyl, methoxycarbonyl, carbamoyl, benzyloxycarbonylamino and halogen.

45

11. A compound of formula (Ia):



(Ia)

wherein:

A is -C(Y)- or -SO<sub>2</sub>-

Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

R<sub>1</sub> is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycle, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>2</sub> is H or alkyl;

R<sub>3</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>3</sub> is optionally substituted by one or more groups of the formula R<sub>d</sub>;

5 R<sub>d</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy, carbamoyl, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

20 R<sub>e</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R<sub>4</sub> is H or alkyl;

R<sub>5</sub> is H, alkyl or cycloalkyl;

30 R<sub>6</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>6</sub> is optionally substituted by one or more groups of the formula R<sub>f</sub>;

35 R<sub>f</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, heteroarylalkoxy, alkoxycarbonyl, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy, carbamoyl, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo,

carboxy, cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

5  $R_g$  is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by halogen, C1-5alkyl or C1-5alkoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkanoylamino, aroylamino, alkylthio wherein the sulfur atom  
10 may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxycarbonylamino, aryloxy, carbamoylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein  
15 the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

20 or  $R_5$  together with  $R_6$  form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more  $R_h$ ;

$R_h$  is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl or heteroaryl; halogen, hydroxy, carboxy and cyano;

$R_7$  is  $R_8-C(Z)-$ ;

30 wherein Z is O, S, or  $NR_i$  wherein  $R_i$  is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy and hydroxy;

$R_8$  is a 5-8 membered monocyclic heteroaryl or 8-11 membered bicyclic heteroaryl ring system, each of the monocyclic or bicyclic ring systems having 1-4 of the same or  
35 different heteroatoms selected from the group consisting of N, O and S wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

$R_j$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, alkoxycarbonyl, aryloxy, alkanoyloxy, aroyloxy, carbamoyl wherein the  
40 nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur  
45 atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl;

alkoxycarbonylamino, aryloxy carbonylamino, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy carbonylamino, arylalkoxy carbonylamino, arylalkoxy carbonylaminoalkyl, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein  $R_k$  may be further optionally substituted by  $R_l$ ;

$R_l$  is selected from the group consisting of alkyl, cycloalkyl, aryl, and benzyl;

X is O, S or N-OH;

and the pharmacutrically acceptable derivatives thereof;

with the following provisos:

when  $R_6$  is alkyl the alkyl must be substituted with  $R_f$  wherein  $R_f$  is not hydroxy, sulfhydryl or halogen;

and

when  $R_1$  is C1alkyl then  $R_b$  cannot be carbamoyl, alkanoylamino, aroylamino, ureido, alkoxycarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, amino, amidino or guanidino wherein each said  $R_b$  is linked to said  $R_1$  via the nitrogen atom thereof.

12. The compound according to claim 11 wherein:

$R_a$  is selected from the group consisting of H, alkyl and aryl;



R<sub>1</sub> is C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_3$  is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,

5 piperazinyl and indolinyl or heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl,  
 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 10 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,  
 quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino,  
 aryloxy carbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy,  
 alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl,  
 amino wherein the nitrogen atom may be independently mono or di-substituted by  
 15 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,  
 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl,  
 20 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,  
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl  
 and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and  
 guanidino,  $R_4$  may be further optionally substituted by one or more  $R_4$ ;

20  $R_4$  is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl,  
 aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen,  
 hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25  $R_5$  is H or alkyl;

$R_6$  is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein  $R_6$  is optionally substituted by one or  
 more  $R_6$ ;

30  $R_f$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from  
 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
 isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,  
 35 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl,  
 isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and  
 phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8  
 alkoxycarbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl  
 40 wherein the nitrogen atom may be independently mono or di-substituted by C1-8  
 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,  
 45 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl,  
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,

quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, C1-3alkyl or C1-3alkoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,

5 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,  
 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
 C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom  
 may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom  
 may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen  
 atom may be independently substituted by alkyl, aryl, heterocyclyl  
 selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 10 thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,  
 tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,  
 indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,  
 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxazinyl,  
 15 alkoxycarbonylamino, aryloxy carbonylamino, C1-8 alkylcarbamoyloxy,  
 arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,  
 alkylaminosulfonyl and arylaminosulfonyl, amino wherein the nitrogen  
 atom may be independently mono or di-substituted by alkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl,  
 20 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or  
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,  
 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 25 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,  
 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,  
 halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

30  $R_h$  is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxycarbonyl,  
 aryloxy carbonyl, arylC1-8alkoxycarbonyl, carbamoyl wherein the nitrogen atom  
 may be optionally mono or di-substituted with a group selected from C1-8 alkyl,  
 C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group  
 35 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl  
 and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,  
 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,  
 indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,  
 40 benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl,  
 carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, carboxy and  
 cyano;

45  $R_8$  is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl,  
 pyrimidinyl, pyrazinyl, triazinyl, indolizynyl, indolyl, isoindolyl, benzofuranyl,

benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, tetrazolyl, purinyl, quinoliziny, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxaliny, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

5 R<sub>j</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy,

oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of alkyl, cycloalkyl, aryl,  
 5 heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;  
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
 oxazoliyl, thiazoliyl, imidazoliyl, isoxazoliyl, isothiazoliyl, oxadiazoliyl,  
 triazoliyl, tetrazoliyl, thiadiazoliyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 10 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazoliyl,  
 benzthiazoliyl, benzoxazoliyl, purinyl, quinolinyl, isoquinolinyl,  
 quinazolinyl, quinoxalinyl, carbazoliyl, phenothiazinyl and phenoxazinyl,  
 alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl,  
 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be  
 15 independantly mono or di-susbstituted by alkyl, aryl, heterocyclyl selected  
 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,  
 thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from  
 furanyl, thienyl, pyrrolyl, oxazoliyl, thiazoliyl, imidazoliyl, isoxazoliyl,  
 isothiazoliyl, oxadiazoliyl, triazoliyl, tetrazoliyl, thiadiazoliyl, pyridinyl,  
 20 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,  
 benzothienyl, benzimidazoliyl, benzthiazoliyl, benzoxazoliyl, purinyl,  
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazoliyl,  
 phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, alkylthio  
 wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio  
 25 wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido  
 wherein either nitrogen atom may be independently substituted by alkyl,  
 aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl,  
 heteroaryl selected from furanyl, thienyl, pyrrolyl, oxazoliyl, thiazoliyl,  
 30 imidazoliyl, isoxazoliyl, isothiazoliyl, oxadiazoliyl, triazoliyl, tetrazoliyl,  
 thiadiazoliyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,  
 isoindolyl, benzofuranyl, benzothienyl, benzimidazoliyl, benzthiazoliyl,  
 benzoxazoliyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,  
 quinoxalinyl, carbazoliyl, phenothiazinyl and phenoxazinyl,  
 35 alkoxycarbonylamino, aryloxycarbonylamino, arylalkoxycarbonylamino,  
 arylalkoxycarbonylaminoalkyl, C1-8 alkylcarbamoyloxy,  
 arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,  
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom  
 may be independently mono or di-susbstituted by alkyl, aryl, heterocyclyl  
 40 selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,  
 piperazinyl and indolinyl, heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazoliyl, thiazoliyl, imidazoliyl, isoxazoliyl,  
 isothiazoliyl, oxadiazoliyl, triazoliyl, tetrazoliyl, thiadiazoliyl, pyridinyl,  
 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,  
 45 benzothienyl, benzimidazoliyl, benzthiazoliyl, benzoxazoliyl, purinyl,  
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazoliyl,

phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein  $R_k$  may be further optionally substituted by  $R_i$ ;

5  $R_i$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl and benzyl;

and

10 X is O or S.

13. The compound according to claim 12 wherein:

15 Y is O or S;

20  $R_1$  is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or  
25 amino wherein  $R_1$  is optionally substituted by one or more  $R_6$ ;

$R_6$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl  
30 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
35 wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
40 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently  
45 substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl



or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5  
 5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkyl sulfonylamino, aryl sulfonylamino, C1-5 alkyl aminosulfonyl, aryl aminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of  
 10 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25  $R_2$  is H or C1-3 alkyl;

$R_3$  is H, C1-5 alkyl, C3-7 cycloalkyl or aryl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

30  $R_d$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkanoyl, aroyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom  
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may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>4</sub> is H or C1-3 alkyl;

R<sub>5</sub> is H or C1-8 alkyl;

R<sub>6</sub> is H, C1-5 alkyl, C3-7 cycloalkyl or aryl wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

R<sub>f</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,

thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoxyloxy, arylcarbamoxyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5

alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_h$  is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, carboxy and cyano;

$R_i$  is alkoxy, aryloxy or hydroxy;

$R_8$  is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliziny, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

$R_j$  is selected from the group consisting of C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl; arylC1-8alkyl, C1-8alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by C1-8alkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8 alkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbtituted by C1-8 alkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by C1-8alkyl, aryl, heterocyclyl selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8alkyl, aryl, heterocyclyl selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkoxycarbonylamino, aryloxycarbonylamino, arylC1-8alkoxycarbonylamino, arylalkoxycarbonylaminoC1-8alkyl, C1-8alkylcarbamoyloxy, arylcarbamoyloxy, C1-8alkylsulfonylamino, arylsulfonylamino, C1-8alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbstituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein  $R_k$  may be further optionally substituted by  $R_l$ .

5 14. The compound according to claim 13 wherein:

Y is O;

10 R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

15 R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

45 R<sub>c</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, and cyano;

R<sub>2</sub> is H or methyl;

R<sub>3</sub> is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl, wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

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R<sub>d</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

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R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

R<sub>4</sub> is H or methyl;

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R<sub>5</sub> is H or C1-5 alkyl;



R<sub>6</sub> is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl or naphthyl wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

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R<sub>f</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

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R<sub>g</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; naphthyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,

pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and  
 quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5  
 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
 5 wherein the nitrogen atom may be independently mono or di-substituted  
 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of  
 piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the  
 group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,  
 imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
 10 benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl,  
 C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom  
 may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom  
 may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen  
 atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl  
 15 selected from the group consisting of piperidinyl, morpholinyl and  
 piperazinyl or heteroaryl selected from the group consisting of furanyl,  
 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,  
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,  
 quinolinyl, isoquinolinyl, C1-5 alkoxycarbonylamino,  
 20 aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5  
 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,  
 arylaminosulfonyl, amino wherein the nitrogen atom may be  
 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl  
 25 selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl and piperazinyl or heteroaryl selected from the group  
 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
 pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen,  
 30 hydroxy, oxo, carboxy and cyano;

35  $R_h$  is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5  
 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein  
 the nitrogen atom may be optionally mono or di-substituted with a group selected  
 from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl  
 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and  
 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
 40 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and  
 isoquinolinyl, halogen, hydroxy, carboxy and cyano;

45 Z is O or S;

$R_8$  is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliziny, quinoliny, isoquinoliny, cinnoliny, phthalazinyl, quinazoliny, quinoxaliny, naphthyridiny, pteridinyl, carbazolyl, acridiny and phenazinyl, wherein  
 5 any of the above  $R_8$  can be optionally substituted by one or more groups of the formula  $R_j$ ;

$R_j$  is selected from the group consisting of C1-5alkyl, C3-6cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group  
 10 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinoliny and  
 15 isoquinoliny, arylC1-5alkyl, C1-5alkoxy, aryloxy, arylC1-5alkoxy, C1-5alkoxycarbonyl, aryloxycarbonyl, C1-5alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by C1-5alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl,  
 20 morpholinyl and piperazinyl, heteroaryl selected from furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinoliny and  
 25 isoquinoliny, C1-5alkanoylamino, aroylamino, C1-5alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-5alkylthio wherein the sulfur  
 30 atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl  
 35 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinoliny and isoquinoliny, C1-5alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,  
 40 arylcarbamoyloxy, C1-5alkylsulfonylamino, arylsulfonylamino, C1-5alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbtituted by C1-5 alkyl, aryl, heterocyclyl  
 45 selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliny  
 and isoquinoliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

$R_k$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected  
 45 from the group consisting of furanyl, thienyl, pyrrolyl, tetrazolyl,

pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, C1-3 alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by C1-3 alkyl, aryl, heterocyclyl selected from the group consisting of morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, and pyridinyl, C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl, phenyl, naphthyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-3alkoxycarbonylamino, aryloxycarbonylamino, arylC1-3alkoxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbstituted by C1-3alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, wherein  $R_k$  may be further optionally substituted by  $R_i$ ;

$R_i$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl and phenyl.

15. The compound according to claim 14 wherein:

$R_1$  is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group

consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
 5 wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur  
 10 atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl or naphthyl; C1-5 alkoxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,  
 15 arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
 20 benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;  
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$R_2$  is H;

$R_3$  is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one  
 30 or more  $R_4$ ;

$R_4$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of  
 35 furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of  
 40 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
 45 independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl

and indolyl, C1-5 alkoxy-carbonylamino, C1-5 alkyl-carbamoyloxy, aryl-carbamoyloxy, C1-5 alkyl-sulfonylamino, aryl-sulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

wherein the configuration at the stereocenter defined by  $R_2$  and  $R_3$  and the carbon they are attached to is L;

$R_4$  is H;

$R_5$  is H or C1-3 alkyl;

$R_6$  is H, C1-5 alkyl, C3-6 cycloalkyl or phenyl. wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxy-carbonyl, aryloxy-carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxy-carbonylamino, C1-5 alkyl-sulfonylamino, aryl-sulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and

piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

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R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; halogen, hydroxy, oxo, carboxy and cyano;

R<sub>h</sub> is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, halogen, hydroxy, carboxy and cyano;

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wherein Z is O;

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R<sub>8</sub> is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;

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R<sub>j</sub> is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, arylC1-

3alkyl, C1-3alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by C1-3alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, morpholinyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-3 alkoxycarbonylamino, aryloxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbstituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy, cyano and nitro, R<sub>j</sub> may be further optionally substituted by one or more R<sub>k</sub>;

R<sub>k</sub> is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyrimidinyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by C1-3 alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; arylC1-3alkoxycarbonylamino, benzyloxycarbonylamino C1-5alkyl, methylcarbamoyloxy, amino wherein the nitrogen atom may be independently mono or di-susbstituted by C1-3alkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, wherein R<sub>k</sub> may be further optionally substituted by R<sub>i</sub>;

R<sub>i</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl and phenyl.



16. The compound according to claim 15 wherein:

5 R<sub>1</sub> is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, or amino, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

10 R<sub>b</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl; C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy and cyano, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

35 R<sub>3</sub> is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

40 R<sub>d</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5

alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_6$  is H, C1-5 alkyl or phenyl wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridyl, C1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

$R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the

nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, phenyl, benzyl, halogen, hydroxy, carboxy and cyano;

- 5 R<sub>8</sub> is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, wherein any of the above R<sub>8</sub> can be optionally substituted by one or more R<sub>j</sub>;
- 10 R<sub>j</sub> is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyrimidinyl, benzyl, C1-3alkoxy, phenoxy, benzyloxy, C1-3alkoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl;
- 15 acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, thiazolyl, imidazolyl and pyridinyl; C1-3
- 20 alkoxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonfylamino, arylsulfonfylamino, amino wherein the nitrogen atom may be independently mono or di-susbstituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl; halogen, hydroxy, carboxy, cyano and nitro, R<sub>j</sub> may be further optionally substituted by one or more
- 25 R<sub>k</sub>;
- R<sub>k</sub> is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyridinyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by methyl, phenyl, furanyl, thienyl; acetylamino, benzoylamino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl and thiazolyl,
- 30 benzyloxycarbonylamino, benzyloxycarbonylamino C1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-susbstituted by C1-3alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl, halogen, hydroxy, carboxy, cyano and nitro, wherein R<sub>k</sub> may be further optionally substituted by R<sub>i</sub>;
- 40 R<sub>i</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl and phenyl.

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17. The compound according to claim 16 wherein:

5  $R_1$  is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyranyl, thiopyranyl or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

10  $R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl;,  
15 halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

20  $R_c$  is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

25  $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3alkoxy, C1-5alkoxycarbonyl, C1-5alkanoyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl; C1-5alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3alkoxycarbonylamino, C1-3alkylsulfonylamino, amino wherein the nitrogen atom may be independently  
30 mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

35  $R_e$  is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_5$  is H or methyl;

40  $R_6$  is C1-5 alkyl or phenyl, wherein  $R_6$  is optionally substituted by one or more groups of the formula  $R_f$ ,

45  $R_f$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom

may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy-carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

5

$R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen or methyl; C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxy-carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5

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alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

15

$R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy-carbonyl, benzyloxy and carboxy;

20

$R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, benzimidazolyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

25

$R_j$  is selected from the group consisting of C1-5 alkyl, cyclohexyl, phenyl, piperidinyl, furanyl, thienyl, pyridinyl, benzyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl; acetylamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, C1-3 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be

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independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy and cyano,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

35

$R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, piperazinyl, furanyl, thienyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetylamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylamino C1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, furanyl, or thienyl; halogen, hydroxy, carboxy, cyano and nitro, wherein  $R_k$  may be further optionally substituted by  $R_l$ ;

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45

$R_l$  is selected from the group consisting of methyl, C3-6 cycloalkyl and phenyl.

5 18. The compound according to claim 7 wherein:

A is -C(O)- or -SO<sub>2</sub>-;

10 R<sub>1</sub> is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

15 R<sub>b</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be  
20 independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, oxo, carboxy and cyano, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy;

25 R<sub>3</sub> is C1-5 alkyl or C5-6 cycloalkyl, wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

30 R<sub>d</sub> is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

35 R<sub>e</sub> is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

40 R<sub>f</sub> is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

45 R<sub>g</sub> is selected from the group consisting of methyl, phenyl optionally substituted by halogen or methyl; methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently

mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy and carboxy;

5  $R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

10  $R_j$  is selected from the group consisting of C1-5 alkyl, phenyl, furanyl, thienyl, piperidinyl, pyridinyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-substituted by methyl or phenyl; acetylamino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl; halogen, hydroxy, carboxy and cyano, 15  $R_j$  may be further optionally substituted by one or more  $R_k$ ; and

20  $R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independantly mono or di-substituted by methyl or phenyl; ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl and thienyl; halogen, hydroxy, carboxy, 25 cyano and nitro, wherein  $R_k$  may be further optionally substituted by  $R_i$ ;

$R_i$  is selected from the group consisting of methyl and phenyl.

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19. The compound according to claim 18 wherein:

35  $R_1$  is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranlyl or thiopyranlyl, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

40  $R_b$  is selected from the group consisting of, pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy and carboxy,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of methoxy, halogen and hydroxy;

45

$R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized

to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

5  $R_e$  is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

$R_5$  is H;

10  $R_f$  is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

15  $R_g$  is selected from the group consisting of methyl, phenyl optionally substituted by halogen; methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

20  $R_8$  is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_8$  can be optionally substituted by one or more  $R_j$ ;

25  $R_j$  is selected from the group consisting of C1-5 alkyl, phenyl, piperidinyl, pyridinyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by methyl or phenyl; methoxycarbonylamino, halogen, hydroxy and carboxy,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

30  $R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, methoxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbstituted by methyl or phenyl; benzyloxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-susbstituted by methyl or phenyl; halogen, hydroxy and carboxy.

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20. The compound according to claim 9 wherein:

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$R_1$  is phenyl or 4-morpholinyl, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

45

$R_b$  is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino,  $R_b$  may be further optionally substituted by a halogen atom;

$R_3$  is C1-5 alkyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;



$R_d$  is selected from the group consisting of C3-6 cycloalkyl and phenyl,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of methyl and halogen;

5

$R_f$  is C1-5 alkyl optionally substituted by one or more  $R_g$ ;

10

$R_f$  is selected from the group consisting of C5-6 cycloalkyl, phenyl, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, and halogen,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy;

15

$R_h$  is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above  $R_h$  can be optionally substituted by one or more  $R_j$ ;

20

$R_j$  is selected from the group consisting of C1-5 alkyl, phenyl, pyridinyl, piperidinyl, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independantly mono or disubstituted by methyl or phenyl; methoxycarbonylamino and halogen,  $R_j$  may be further optionally substituted by one or more  $R_k$ ;

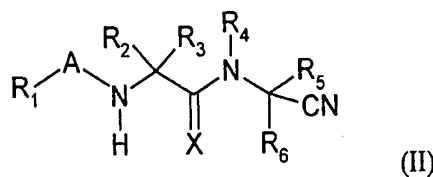
25

$R_k$  is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, methoxycarbonyl, carbamoyl, benzyloxycarbonylamino and halogen.

30

21. A compound of the formula (II):

35



wherein:

40

A is -C(Y)- or -SO<sub>2</sub>-

Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

- 5 R<sub>1</sub> is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

10 R<sub>b</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, 15 aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, 20 nitro, amidino and guanidino; R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

25 R<sub>c</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

30 R<sub>2</sub> is H or alkyl;

35 R<sub>3</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

40 R<sub>d</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, 45 aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano,

nitro, amidino and guanidino,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

5  $R_e$  is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

10  $R_d$  is H or alkyl;

$R_s$  is H or alkyl;

15  $R_6$  is H, alkyl, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl or cyano, wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

20  $R_f$  is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, heteroarylalkoxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

35  $R_g$  is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino,

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arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5

or  $R_5$  together with  $R_6$  form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more  $R_h$ ;

10  $R_h$  is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxy carbonyl, arylalkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heteroaryl, halogen, hydroxy, carboxy and cyano;

15

X is O, S or N-OH; and  
the pharmaceutically acceptable derivatives thereof;

with the proviso that when Y is O and  $R_6$  is arylalkyl or heteroarylalkyl then  $R_1$  cannot  
20 be alkyl, cycloalkyl, aryl, heteroaryl, cycloalkyl-alkyl, aryl-alkyl or aryl-cycloalkyl.

25

22. The compound according to claim 21 wherein:

Y is O, S or  $NR_a$  wherein  $R_a$  is H, alkyl or aryl;

30

$R_1$  is C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl,  
35 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalyl, carbazolyl, phenothiazinyl, phenoxazinyl, and amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

40

$R_b$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
45 pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,

benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino;  $R_6$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_3$  is H, C1-8 alkyl, C3-7 cycloalkyl, aryl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

R<sub>d</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from  
 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
 5 pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl,  
 pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl,  
 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8  
 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8  
 10 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be  
 independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected  
 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,  
 thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group  
 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl,  
 15 isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,  
 pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl,  
 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8  
 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be  
 20 oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be  
 oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
 independently substituted by alkyl, aryl, heterocyclyl selected from the group  
 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl  
 and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,  
 25 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl,  
 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,  
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
 benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl,  
 carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino,  
 30 aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy,  
 alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl,  
 amino wherein the nitrogen atom may be independently mono or di-substituted by  
 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl  
 35 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,  
 tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,  
 isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl,  
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl  
 40 and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino,  
 guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl,  
 aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen,  
 45 hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>6</sub> is H, C1-8 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

5 R<sub>f</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, 10 benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, 15 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, 20 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of 30 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, 35 alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, 40 thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and 45 guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

$R_g$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,



quinoxaliny, carbazolyl, phenothiaziny and phenoxaziny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, and guanidino;

5         $R_h$  is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy, carbonyl, aryloxy, carbonyl, arylC1-8alkoxy, carbonyl, carbonyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiaziny and phenoxaziny, halogen, hydroxy, carboxy, and cyano; and

X is O or S.

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23. The compound according to claim 22 wherein:

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Y is O or S;

30         $R_1$  is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny or amino; wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

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40         $R_b$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5 alkoxy, carbonyl, aryloxy, carbonyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl

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selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_2$  is H or C1-3 alkyl;

$R_3$  is H, C1-5 alkyl, C3-7 cycloalkyl, aryl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5alkanoyl, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_4$  is H or C1-3 alkyl

$R_5$  is H or C1-8 alkyl

$R_6$  is H, C1-5 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein  $R_6$  is optionally substituted by one or more  $R_6$ ;

$R_f$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy,

heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,

pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and  
quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein  
the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein  
the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein  
either nitrogen atom may be independently substituted by C1-5 alkyl, aryl,  
heterocyclyl selected from the group consisting of pyrrolidinyl,  
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or  
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,  
pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl,  
C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5  
alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,  
arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino  
wherein the nitrogen atom may be independently mono or di-substituted  
by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of  
pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and  
indolinyl, or heteroaryl selected from the group consisting of furanyl,  
thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,  
pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and  
quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and  
guanidino;

$R_n$  is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl,  
aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom  
may be optionally mono or di-substituted with a group selected from C1-5 alkyl,  
C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group  
consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl  
and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,  
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,  
pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen,  
hydroxy, carboxy and cyano.

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24. The compound according to claim 23 wherein:

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Y is O;

R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl; or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy and cyano;

R<sub>2</sub> is H or methyl;

R<sub>3</sub> is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

R<sub>d</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of

furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,  
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and  
 isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl,  
 aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen  
 atom may be independently mono or di-substituted by C1-5 alkyl, aryl,  
 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,  
 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,  
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and  
 isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur  
 atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom  
 may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom  
 may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl  
 selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or  
 heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
 benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5  
 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be  
 independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl,  
 heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and  
 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,  
 halogen, hydroxy, oxo, carboxy and cyano,  $R_4$  may be further optionally  
 substituted by one or more  $R_c$ .

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,  
 aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino,  
 halogen, hydroxy, oxo, carboxy and cyano;

$R_4$  is H or methyl;

$R_5$  is H or C1-5 alkyl;

$R_6$  is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl or cyano, wherein  $R_6$  is optionally  
 substituted by one or more  $R_f$ .

$R_f$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,  
 naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,

indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny, isoquinoliny, quinazoliny and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny and isoquinoliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny and isoquinoliny, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny and isoquinoliny, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen, methyl or methoxy, naphthyl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indoliny; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny, isoquinoliny, quinazoliny and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,



5 benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, 10 C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano; 20

25  $R_h$  is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, 30 halogen, hydroxy, carboxy and cyano; and

35 X is O.

40 25. The compound according to claim 24 wherein:

Y is O;

45  $R_1$  is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,

imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl or amino, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

5 R<sub>b</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, 10 quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 15 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5 20 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl 25 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

30 R<sub>c</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

R<sub>2</sub> is H;

35 R<sub>3</sub> is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

40 R<sub>d</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen 45 atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl,

5 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,  
 C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be  
 oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be  
 10 oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
 independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group  
 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl  
 and indolyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy,  
 arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein  
 15 the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl,  
 phenyl, heterocyclyl selected from the group consisting of piperidinyl,  
 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of  
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,  
 halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally  
 20 substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl,  
 phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy,  
 aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

25  $R_4$  is H;

$R_6$  is H, C1-5 alkyl, C3-6 cycloalkyl, phenyl or cyano, wherein  $R_6$  is optionally  
 30 substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl,  
 naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
 piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group  
 35 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl,  
 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl  
 and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, heteroarylC1-3alkoxy,  
 C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
 wherein the nitrogen atom may be independently mono or di-substituted by C1-5  
 40 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5  
 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be  
 oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be  
 oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may  
 45 be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
 independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino,  
 C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom  
 may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl,  
 heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and  
 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, halogen, hydroxy,

oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, halogen, hydroxy, oxo, carboxy and cyano;

R<sub>h</sub> is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl or arylC1-3alkyl; halogen, hydroxy, carboxy and cyano.

26. The compound according to claim 25 wherein:

R<sub>i</sub> is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl or amino, wherein R<sub>i</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3

alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

$R_3$  is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_5$  is H or C1-3alkyl;

$R_6$  is H, C1-5 alkyl, phenyl or cyano, wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy,

benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3  
alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aryloxy, carbamoyl  
wherein the nitrogen atom may be independently mono or di-substituted by C1-3  
alkyl or phenyl, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur  
atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur  
atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen  
atom may be independently substituted by C1-5 alkyl or phenyl, C1-3  
alkoxycarbonylamino, amino wherein the nitrogen atom may be independently  
mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy  
and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally  
substituted by one or more groups selected from the group consisting of  
halogen and methyl, heterocyclyl selected from the group consisting of  
piperidiny, morpholinyl and piperazinyl; heteroaryl selected from the  
group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy,  
aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aryloxy,  
carbamoyl wherein the nitrogen atom may be independently mono or di-  
substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-  
5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or  
sulfone, ureido wherein either nitrogen atom may be independently  
substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5  
alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino,  
arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino  
wherein the nitrogen atom may be independently mono or di-substituted  
by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

$R_h$  is selected from the group consisting of C1-3 alkyl, phenyl, C1-3  
alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the  
nitrogen atom may be optionally mono or di-substituted with a group selected  
from the group consisting of C1-5 alkyl, phenyl and benzyl, halogen, hydroxy,  
carboxy and cyano.

27. The compound according to claim 26 wherein:

$R_i$  is C5-6 cycloalkyl, phenyl, naphthyl, piperidiny, morpholinyl, piperazinyl, pyranly,  
thiopyranly, furanyl, thienyl, pyrrolyl or amino, wherein  $R_i$  is optionally substituted by  
one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5

5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

10  $R_c$  is selected from the group consisting of C1-3alkyl, C1-3alkoxy, halogen and hydroxy;

$R_3$  is C1-5 alkyl, C5-6 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more groups of the formula  $R_d$ ;

15  $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5

20 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, C1-3 alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

25  $R_e$  is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

wherein the configuration at the stereocenter defined by  $R_2$  and  $R_3$  and the carbon they are attached to is defined as L;

30

$R_5$  is H or methyl;

$R_6$  is C1-5 alkyl, phenyl or cyano wherein  $R_6$  is optionally substituted by one or more groups of the formula  $R_f$ ;

35

$R_f$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

45

R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

R<sub>h</sub> is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, benzyloxy and carboxy.

28. The compound according to claim 27 wherein:

R<sub>i</sub> is cyclohexyl, phenyl, naphthyl, piperidiny, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino wherein R<sub>i</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy,

R<sub>3</sub> is C1-5 alkyl or C5-6 cycloalkyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

R<sub>d</sub> is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;



$R_6$  is C1-5 alkyl or phenyl, wherein  $R_6$  is optionally substituted by one or more  $R_7$ ;

5  $R_7$  is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently  
10 mono or di-substituted by C1-3 alkyl, halogen, hydroxy, carboxy and cyano,  $R_7$  may be further optionally substituted by one or more  $R_8$ ;

10  $R_8$  is selected from the group consisting of methyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the  
15 nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy and carboxy;

20  $R_9$  is selected from the group consisting of vinyl, phenyl, methoxycarbonyl, benzyloxycarbonyl and carboxy;

25 29. The compound according to claim 28 wherein:

$R_1$  is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein  $R_1$  is optionally substituted by one or more  $R_6$ ;

30

$R_b$  is selected from the group consisting of pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy and carboxy,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

35

$R_c$  is selected from the group consisting of methoxy, halogen and hydroxy;

$R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

40

$R_e$  is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

45  $R_5$  is H;

R<sub>f</sub> is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of methyl, phenyl optionally substituted by halogen, methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

R<sub>h</sub> is vinyl or phenyl.

30. The compound according to claim 29 wherein:

R<sub>1</sub> is phenyl, naphthyl or 4-morpholinyl wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino R<sub>b</sub> may be further optionally substituted by R<sub>c</sub> wherein R<sub>c</sub> is a halogen atom;

R<sub>3</sub> is C1-5 alkyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

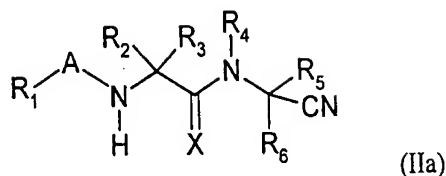
R<sub>d</sub> is selected from the group consisting of C3-6 cycloalkyl, phenyl or naphthyl, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

R<sub>e</sub> is selected from the group consisting of methyl and halogen,

R<sub>f</sub> is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, indolyl, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen and carboxy, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy.

31. A compound of the formula (IIa):



wherein:

A is -C(Y)- or -SO<sub>2</sub>-

Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

R<sub>1</sub> is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxy carbonylamino, aryloxy carbonylamino, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino; R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>2</sub> is H or alkyl;

5 R<sub>3</sub> is H, C2-8alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R<sub>3</sub> is optionally substituted by one or more R<sub>4</sub>;

10 R<sub>4</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, 15 aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>4</sub> may be further optionally substituted by one or 20 more R<sub>c</sub>;

25 R<sub>c</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>4</sub> is H or alkyl;

30 R<sub>5</sub> is H or alkyl;

35 R<sub>6</sub> is H, alkyl, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

40 R<sub>f</sub> is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, heteroarylalkoxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by 45 alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy,

alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

or  $R_5$  and  $R_6$  together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more  $R_h$ ;

$R_h$  is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxy carbonyl, arylalkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heteroaryl, halogen, hydroxy, carboxy and cyano;

X is O, S or N-OH;

and the pharmaceutically acceptable derivatives thereof;

with the following provisos:

when Y is O and  $R_6$  is arylalkyl or heteroarylalkyl then  $R_1$  cannot be alkyl, cycloalkyl, aryl, heteroaryl, cycloalkyl-alkyl, aryl-alkyl or aryl-cycloalkyl;

when  $R_5$  is H then  $R_6$  cannot be H;  
and

when R<sub>1</sub> is C1alkyl then R<sub>b</sub> cannot be carbamoyl, alkanoylamino, aroylamino, ureido, alkoxycarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, amino, amidino or guanidino wherein each said R<sub>b</sub> is linked to said R<sub>1</sub> via the nitrogen atom thereof.

32. The compound according to claim 31 wherein:

Y is O, S or NR<sub>a</sub> wherein R<sub>a</sub> is H, alkyl or aryl;

R<sub>1</sub> is C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl, phenoxazinyl, and amino wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,

imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxazinyl, alkoxycarbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino;  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_3$  is H, C2-8 alkyl, C3-7 cycloalkyl, aryl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be

oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, arylloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino, R<sub>d</sub> may be further optionally substituted by one or more R<sub>c</sub>;

R<sub>c</sub> is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R<sub>6</sub> is H, C1-8 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

R<sub>f</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxycarbonyl, arylloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,



thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

R<sub>g</sub> is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,

pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoxyloxy, arylcarbamoxyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, and guanidino;

or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

R<sub>h</sub> is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxycarbonyl, aryloxycarbonyl, arylC1-8alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, carboxy, and cyano; and

X is O or S.

5 33. The compound according to claim 32 wherein:

Y is O or S;

10 R<sub>1</sub> is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
15 benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or amino; wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
20 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5  
25 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl  
30 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido  
35 wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl,  
40 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkyl sulfonylamino, aryl sulfonylamino, C1-5 alkyl aminosulfonyl, aryl aminosulfonyl, amino wherein the nitrogen atom may be independently mono  
45 or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl,

or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo,  
5 carboxy, cyano, nitro, amidino and guanidino,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro,  
10 amidino and guanidino;

$R_2$  is H or C1-3 alkyl;

$R_3$  is H, C2-5 alkyl, C3-7 cycloalkyl, aryl wherein  $R_3$  is optionally substituted by one or  
15 more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from  
20 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5alkanoyl, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl  
25 wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
30 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido  
35 wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl,  
40 quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group  
45 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl,

pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,  
pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen,  
hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_4$  may be further  
optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,  
aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino,  
halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

$R_4$  is H or C1-3 alkyl

$R_5$  is H or C1-8 alkyl

$R_6$  is H, C1-5 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein  $R_6$  is optionally substituted  
by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl,  
heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,  
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from  
the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl,  
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl,  
quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy,  
heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy,  
aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or  
di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting  
of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and  
indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,  
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,  
pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5  
alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be  
oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be  
oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may  
be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the  
group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,  
piperazinyl and indolinyl or heteroaryl selected from the group consisting of  
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,  
pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,  
benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and

quinoxaliny, C1-5 alkoxy-carbonylamino, aryloxy-carbonylamino, C1-5 alkyl-carbamoyloxy, aryl-carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazoliny and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazoliny and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxy-carbonyl, aryloxy-carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazoliny and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazoliny and quinoxaliny, C1-5 alkoxy-carbonylamino, aryloxy-carbonylamino, C1-5 alkyl-carbamoyloxy, aryl-carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and

indoliny, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

or  $R_5$  and  $R_6$  together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more  $R_h$ ;

$R_h$  is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxy carbonyl, aryloxy carbonyl, arylC1-5 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, arylC1-5 alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indoliny, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, carboxy and cyano.

34. The compound according to claim 33 wherein:

Y is O;

$R_1$  is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl; or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indoliny; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indoliny, or

heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy and cyano;

$R_2$  is H or methyl;

$R_3$  is H, C2-5 alkyl, C3-7 cycloalkyl or phenyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5



alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,  
arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be  
independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl,  
heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and  
piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,  
halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally  
substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,  
aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino,  
halogen, hydroxy, oxo, carboxy and cyano;

$R_4$  is H or methyl;

$R_5$  is H or C1-5 alkyl;

$R_6$  is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl or cyano, wherein  $R_6$  is optionally  
substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,  
naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,  
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,  
indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl,  
isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-  
5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5  
alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be  
independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected  
from the group consisting of piperidinyl, morpholinyl and piperazinyl or  
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,  
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,  
aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a  
sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a  
sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized  
to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the  
group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl  
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5  
alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,  
arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5  
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be  
5 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected  
from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and  
piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,  
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,  
10 halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally  
substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl,  
phenyl optionally substituted by one or more groups selected from  
15 halogen, methyl or methoxy, naphthyl optionally substituted by one or  
more groups selected from halogen, methyl or methoxy, heterocyclyl  
selected from the group consisting of pyrrolidinyl, piperidinyl,  
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl  
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
20 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,  
pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny,  
C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl,  
aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the  
25 nitrogen atom may be independently mono or di-substituted by C1-5 alkyl,  
aryl, heterocyclyl selected from the group consisting of piperidinyl,  
morpholinyl and piperazinyl or heteroaryl selected from the group  
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,  
pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,  
30 benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,  
aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a  
sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a  
sulfoxide or sulfone, ureido wherein either nitrogen atom may be  
independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from  
35 the group consisting of piperidinyl, morpholinyl and piperazinyl or  
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,  
oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,  
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,  
C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5  
40 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,  
arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino  
wherein the nitrogen atom may be independently mono or di-substituted  
by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of  
pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl  
45 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,  
thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;

or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>n</sub>;

R<sub>n</sub> is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, arylC1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3 alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano; and

X is O.

35. The compound according to claim 34 wherein:

Y is O;

R<sub>1</sub> is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl or amino, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>6</sub>;

R<sub>6</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be

oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5 alkoxy, carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

$R_2$  is H;

$R_3$  is C2-5 alkyl, C3-6 cycloalkyl or phenyl, wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxy, carbonyl, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkoxy, carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

R<sub>e</sub> is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

5

R<sub>4</sub> is H;

R<sub>6</sub> is H, C1-5 alkyl, C3-6 cycloalkyl, phenyl or cyano, wherein R<sub>6</sub> is optionally substituted by one or more R<sub>f</sub>;

10

R<sub>f</sub> is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, heteroarylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

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R<sub>g</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl, C1-5

alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, halogen, hydroxy, oxo, carboxy and cyano;

or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

R<sub>h</sub> is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl or arylC1-3alkyl; halogen, hydroxy, carboxy and cyano.

36. The compound according to claim 35 wherein:

R<sub>i</sub> is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl or amino, wherein R<sub>i</sub> is optionally substituted by one or more R<sub>b</sub>;

R<sub>b</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl

and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

5  $R_c$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

$R_3$  is C2-5 alkyl, C5-6 cycloalkyl or phenyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

10  $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5  
15 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy,  
20 oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen,  
25 hydroxy, oxo, carboxy and cyano;

$R_5$  is H or C1-3alkyl;

30  $R_6$  is H, C1-5 alkyl, phenyl or cyano, wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3  
35 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen  
40 atom may be independently substituted by C1-5 alkyl or phenyl, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

45  $R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from the group consisting of

5 halogen and methyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

15 or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

20 R<sub>h</sub> is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy carbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from the group consisting of C1-5 alkyl, phenyl and benzyl, halogen, hydroxy, carboxy and cyano.

25

37. The compound according to claim 36 wherein:

30 R<sub>1</sub> is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl or amino, wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

35 R<sub>b</sub> is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>b</sub> may be further optionally substituted by one or more R<sub>c</sub>;

40 R<sub>c</sub> is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

45



or more groups of the formula  $R_d$ ,  
 $R_d$  is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, C1-5 alkoxy carbonyl, C1-5 alkanoyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy carbonylamino, C1-3 alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl

$R_c$  is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

R<sub>5</sub> is H or methyl;

R<sub>f</sub> is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>.

35  $R_g$  is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

40 or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>n</sub>;

45 R<sub>h</sub> is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy carbonyl, benzyloxy and carboxy.

38. The compound according to claim 37 wherein:

$R_1$  is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, oxo, carboxy and cyano,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy,

$R_3$  is C2-5 alkyl or C5-6 cycloalkyl wherein  $R_3$  is optionally substituted by one or more  $R_d$ ;

$R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

$R_6$  is C1-5 alkyl or phenyl, wherein  $R_6$  is optionally substituted by one or more  $R_f$ ;

$R_f$  is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of methyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy and carboxy;

or  $R_5$  and  $R_6$  together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more  $R_h$ ;

$R_h$  is selected from the group consisting of vinyl, phenyl, methoxycarbonyl, benzyloxycarbonyl and carboxy;

39. The compound according to claim 38 wherein:

$R_1$  is cyclohexyl, phenyl, naphthyl, piperidiny, morpholinyl, piperazinyl, pyranly or thiopyranly, wherein  $R_1$  is optionally substituted by one or more  $R_b$ ;

$R_b$  is selected from the group consisting of pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy and carboxy,  $R_b$  may be further optionally substituted by one or more  $R_c$ ;

$R_c$  is selected from the group consisting of methoxy, halogen and hydroxy;

$R_d$  is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano,  $R_d$  may be further optionally substituted by one or more  $R_e$ ;

$R_e$  is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

$R_5$  is H;

$R_f$  is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano,  $R_f$  may be further optionally substituted by one or more  $R_g$ ;

$R_g$  is selected from the group consisting of methyl, phenyl optionally substituted by halogen, methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

or R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>;

R<sub>h</sub> is vinyl or phenyl.

5

40. The compound according to claim 39 wherein:

10

R<sub>1</sub> is phenyl, naphthyl or 4-morpholinyl wherein R<sub>1</sub> is optionally substituted by one or more R<sub>b</sub>;

15

R<sub>b</sub> is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino R<sub>b</sub> may be further optionally substituted by R<sub>c</sub> wherein R<sub>c</sub> is a halogen atom;

20

R<sub>3</sub> is C2-5 alkyl wherein R<sub>3</sub> is optionally substituted by one or more R<sub>d</sub>;

R<sub>d</sub> is selected from the group consisting of C3-6 cycloalkyl, phenyl or naphthyl, R<sub>d</sub> may be further optionally substituted by one or more R<sub>e</sub>;

25

R<sub>e</sub> is selected from the group consisting of methyl and halogen,

30

R<sub>f</sub> is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, indolyl, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen and carboxy, R<sub>f</sub> may be further optionally substituted by one or more R<sub>g</sub>;

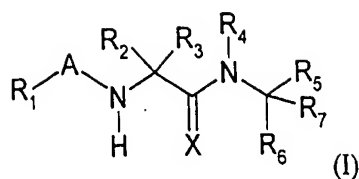
35

R<sub>g</sub> is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy, and

R<sub>5</sub> and R<sub>6</sub> together with the carbon they are attached form a carbocyclic ring of 3 carbon atoms, the carbocyclic ring being optionally substituted with one or more R<sub>h</sub>.

40

41. A method of making a compound of the formula(I) comprising:

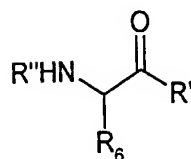


wherein A is  $-C(O)-$ , X is O,  $R_7$  is  $R_8-C(O)-$  and  $R_2, R_3, R_6$  and  $R_8$  are as defined in claim

1;

a) coupling a protected amino acid with N,O-dimethylhydroxylamine under coupling

5 conditions in a suitable solvent to give the corresponding amide below:



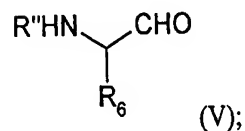
wherein  $R''$  is an amino protecting group,  $R'$  is  $NMe(OMe)$  and  $R_6$  is as defined in claim

1;

10

b) reducing the compound produced in a step a) with a reducing agent in a suitable

solvent to form a compound of the formula (V):



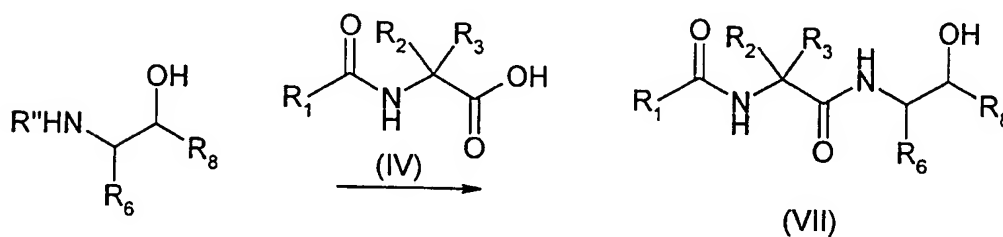
15

d) reacting a heterocycle  $R_8$  according to claim 1, with  $n-BuLi$  to form a corresponding

heterocyclic anion in a suitable solvent at a temperature about  $-30$  to  $-100^\circ C$ ; reacting

the heterocycle  $R_8$  anion with a compound of formula V;

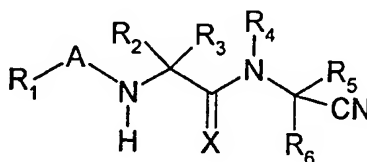
- e) removing the protecting group R" from the compound produced in step d) and subsequently coupling with a compound of the formula (IV) under coupling conditions to produce a compound of the formula (VII):



and

- f) oxidizing compound VII from step e) to produce a compound of the formula (I).

42. A method of making a compound of the formula (II) comprising:

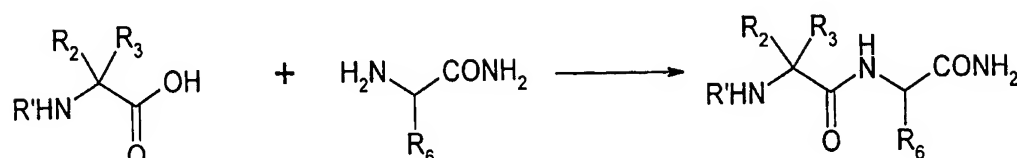


(II)

wherein A is -C(O)-, X is O, and R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> are as defined in claim 21;

- a) coupling under coupling conditions a protected amino acid with a protecting group R' with an amide compound possessing R<sub>6</sub>:

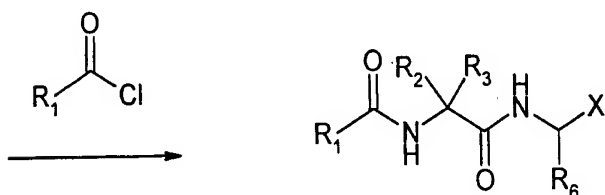
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10

- b) removing the protecting group R' from the compound produced in step a);
- c) reacting the compound produced from step b) with an acid chloride according to the formula below:

15



wherein X' is CONH<sub>2</sub> and R<sub>1</sub> is as defined in claim 21;

and

- d) dehydrating the amide compound produced in step c) with a dehydrating agent under suitable dehydrating conditions to produce the nitrile compound of the formula(II).

20

43. A compound selected from the group consisting of:

*N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*S*-cyano-3-phenylpropyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;

*N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2*R*-benzyloxypropyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-chlorophenyl)methoxyethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-chlorophenyl)methoxyethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methoxyphenyl)methoxyethyl)amide;

*N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfonyl)ethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfinyl)ethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-methoxyphenyl)methylsulfanyl)ethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-chlorophenyl)methoxyethyl)amide;

*N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-methylphenyl)methoxyethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methylphenyl)methoxyethyl)amide;

*N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-methylphenyl)methoxyethyl)amide;



- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-carbomethoxyphenyl)methoxyethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-carbomethoxyphenyl)methoxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbo-*t*-butoxy)propyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*S*-(benzthiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 15 *N*-(4-Morpholinecarbonyl)-L-leucine [1*S*-cyano-5-((benzyloxycarbonyl)-amino)-pentyl]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,*S*-(benzoxazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine [[1-[(6-phenylcarbonyl)benzothiazol-2-ylcarbonyl]-3-phenylpropyl]]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[[6-(carbomethoxy)-benzoxazol-2-ylcarbonyl]-3-phenylpropyl]amide;
- 25 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-nor-leucine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine 1*RS*-[(5-phenyloxazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 35 *N*-(4-Morpholinecarbonyl)-L-leucine 1*S*-(oxazol-2-ylcarbonyl)-3-phenylpropylamide;
- N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 40 *N*-(4-morpholinecarbonyl)-L-(2-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(2-chlorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 45 *N*-Benzoyl-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;

- N*-(4-morpholinecarbonyl)-L-(O-methyl)tyrosine (1*S*-cyano-3-phenylpropyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;  
 5    *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-1-phenylmethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1-cyanocyclopropyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;  
 10    *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-(2,6-dichloromethyloxy)phenyl)ethyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;  
 15    *N*-(4-morpholinecarbonyl)-L-leucine (1*S*,3-dicyanopropyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*,2-dicyanoethyl)amide;  
 20    *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;  
*N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-cyclohexylethyl)amide and  
 25    pharmaceutically acceptable derivatives thereof.

44.    A compound selected from the group consisting of:

- 30    Morpholine-4-carboxylic acid {1-(*S*)-[1(*S*)-(2,4-diphenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethylbutyl} amide;  
       Morpholine-4-carboxylic acid {2-cyclohexyl-1-(*S*)-[1-(*S*)-(2,4-diphenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl} amide;  
 35    Morpholine-4-carboxylic acid {1-(*S*)-[2,4-diphenyl-oxazole-5-yl)-2-oxo-ethylcarbamoyl]-3-methylbutyl} amide;  
       Morpholine-4-carboxylic acid {2-cyclohexyl-1-(*S*)-[2-(2,4-diphenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl}-amide;  
 40

Morpholine-4-carboxylic acid {1-(S)-[2-(2,4-diphenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3,3-dimethylbutyl}-amide;

5 Morpholine-4-carboxylic acid (1-(S)-{1-(S)-[2-(3-benzyloxy-phenyl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide;

Morpholine-4-carboxylic acid {2-cyclohexyl-1-(S)-[1-(R,S)-(4-isobutyl-2-pyridin-2-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl} amide and

10 the pharmaceutically acceptable derivatives thereof.

45. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound according to claims 1, 11, 21, 31 or 43.

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46. A method of modulating an autoimmune disease, said method comprising administering to a patient in need of such treatment a pharmaceutically effective amount of a compound according to claims 1, 11, 21, 31 or 43.

20 47. The method according to claim 46 wherein the autoimmune disease is selected from the group consisting of: rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, multiple sclerosis, Guillain-Barre syndrome, psoriasis, Grave's disease, myasthenia gravis, scleroderma, glomerulonephritis, atopic dermatitis and insulin-dependent diabetes mellitus.

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48. A method of treating Alzheimer's disease comprising administering to a patient in need of such treatment a pharmaceutically effective amount of a compound according to claims 1, 11, 21, 31 or 43.

49. A method of treating atherosclerosis comprising administering to a patient in need of such treatment a pharmaceutically effective amount of a compound according to claims 1, 11, 21, 31 or 43.

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/26278

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D277/64 C07D263/32 C07D413/04 C07D295/20 C07C311/42  
 A61P9/10 A61P25/28 A61P37/02

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07C A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 113, no. 21, 19 November 1990 (1990-11-19) Columbus, Ohio, US; abstract no. 187051, HANZLIK, ROBERT P. ET AL: "Reversible covalent binding of peptide nitriles to papain" XP002129208 cited in the application abstract & BIOCHIM. BIOPHYS. ACTA (1990), 1035(1), 62-70 , --- -/--	21-49

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

28 January 2000

Date of mailing of the international search report

14/02/2000

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 102, no. 1, 7 January 1985 (1985-01-07) Columbus, Ohio, US; abstract no. 2545, CAREY, PAUL R. ET AL: "Identity of acyl group conformations in the active sites of papain and cathepsin B by resonance Raman spectroscopy" XP002129209 abstract & J. BIOL. CHEM. (1984), 259(23), 14357-60 ,	21-49
X	DUFOUR, ERIC ET AL: "Engineering nitrile hydratase activity into a cysteine protease by a single mutation" BIOCHEMISTRY (1995), 34(50), 16382-8 , XP002129204 page 16384 -page 16387 ---	21-49
X	CHEMICAL ABSTRACTS, vol. 120, no. 23, 6 June 1994 (1994-06-06) Columbus, Ohio, US; abstract no. 292661, LIU, SIMING ET AL: "The contribution of intermolecular hydrogen bonding to the kinetic specificity of papain" XP002129210 abstract & BIOCHIM. BIOPHYS. ACTA (1993), 1158(3), 264-72 , ---	21-49
X	GOUR-SALIN, BARBARA J. ET AL: "Inhibition of papain by peptide nitriles: conversion of the nitrile group into other functionalities via the papain:nitrile thioimide ester adduct" CAN. J. CHEM. (1991), 69(8), 1288-97 , XP002129205 cited in the application page 1289 -page 1291 ---	21-49
X	CHEMICAL ABSTRACTS, vol. 113, no. 21, 19 November 1990 (1990-11-19) Columbus, Ohio, US; abstract no. 187051, HANZLIK, ROBERT P. ET AL: "Reversible covalent binding of peptide nitriles to papain" XP002129211 cited in the application abstract & BIOCHIM. BIOPHYS. ACTA (1990), 1035(1), 62-70 , ---	21-49
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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/26278

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 111, no. 15, 9 October 1989 (1989-10-09) Columbus, Ohio, US; abstract no. 129491, BUTTLE, DAVID J. ET AL: "Affinity purification of the novel cysteine proteinase papaya proteinase IV, and papain from papaya latex" XP002129212 abstract & BIOCHEM. J. (1989), 261(2), 469-76 , ---	21-49
X	CHEMICAL ABSTRACTS, vol. 107, no. 1, 6 July 1987 (1987-07-06) Columbus, Ohio, US; abstract no. 3097, LIANG, TZYY CHYAU ET AL: "Inhibition of papain by nitriles: mechanistic studies using NMR and kinetic measurements" XP002129213 abstract & ARCH. BIOCHEM. BIOPHYS. (1987), 252(2), 626-34 , ---	21-49
X	MOON, JOSEPH B. ET AL: "Reversible covalent inhibition of papain by a peptide nitrile. Carbon-13 NMR evidence for a thioimide ester adduct" J. AM. CHEM. SOC. (1986), 108(6), 1350-1 , XP002129206 the whole document ---	21-49
X	ASBOTH, BENICE ET AL: "Mechanism of action of cysteine proteinases: oxyanion binding site is not essential in the hydrolysis of specific substrates" BIOCHEMISTRY (1985), 24(3), 606-9 , XP002129207 page 607 ---	21-49
X	WO 92 17453 A (DU PONT MERCK PHARMA) 15 October 1992 (1992-10-15) * see the examples * ---	21-49
X	WO 95 24382 A (SEARLE & CO ;HALLINAN E ANN (US); TJOENG FOE S (US); FOK KAM F (US) 14 September 1995 (1995-09-14) the whole document ---	21-49
X	WO 97 27220 A (BASF AG ;PARKE DAVIS (US)) 31 July 1997 (1997-07-31) page 11-12 ---	21-49
	-/--	

# INTERNATIONAL SEARCH REPORT

Int. l. Application No  
PCT/US 99/26278

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 09838 A (MERRELL DOW PHARMA ; SCOIS NOVA INC (US); CORDELL BARBARA (US); SCH) 13 April 1995 (1995-04-13) * see the examples *	1
A	WO 95 15749 A (PROTOTEK INC) 15 June 1995 (1995-06-15) * see the claims and the examples *	1
A	WO 96 40647 A (PROTOTEK INC) 19 December 1996 (1996-12-19) * see the examples *	1
A	US 5 691 368 A (PEET NORTON P ET AL) 25 November 1997 (1997-11-25) * see the examples *	1
P, X	WO 99 24460 A (NOVARTIS ERFINDUNGEN VERWALTUN ; ALTMANN EVA (CH); LATTMANN RENE (C) 20 May 1999 (1999-05-20) * see the examples * abstract; claim 1	1-49



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.2

Present claims 1-42, 45-49 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds as displayed by formula (I) on page 175, wherein R1 is a 4-morpholino substituent, and compounds as displayed by formula (II) on page 247, the compounds as mentioned in the description on pages 129-146, the examples on pages 157-167 and the "prophetic" compounds on pages 171 and 174.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/26278

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9217453 A	15-10-1992	US 5206249 A AU 666847 B AU 1767692 A CZ 9302060 A EP 0506008 A EP 0577753 A FI 934225 A HU 68969 A IL 101380 A JP 6506229 T MX 9201355 A NO 933455 A,B, NZ 242126 A SK 107193 A RU 2066316 C US 5329048 A US 5461176 A ZA 9202252 A LV 10045 A,B	27-04-1993 29-02-1996 02-11-1992 16-03-1994 30-09-1992 12-01-1994 15-10-1993 28-08-1995 31-10-1996 14-07-1994 01-10-1992 26-11-1993 25-09-1996 10-08-1994 10-09-1996 12-07-1994 24-10-1993 27-09-1993 10-05-1994
WO 9524382 A	14-09-1995	AU 2115695 A CA 2184691 A EP 0749418 A	25-09-1995 14-09-1995 27-12-1996
WO 9727220 A	31-07-1997	AU 2114197 A CA 2243497 A EP 0880542 A	20-08-1997 31-07-1997 02-12-1998
WO 9509838 A	13-04-1995	AU 687449 B AU 7799894 A CA 2171882 A CN 1132504 A EP 0721449 A FI 961438 A HU 74004 A IL 111078 A JP 9505281 T NO 961326 A NZ 274074 A US 5977074 A ZA 9407529 A	26-02-1998 01-05-1995 13-04-1995 02-10-1996 17-07-1996 29-03-1996 28-10-1996 12-03-1999 27-05-1997 01-04-1996 24-11-1997 02-11-1999 29-05-1995
WO 9515749 A	15-06-1995	US 5486623 A AU 1266495 A CA 2177495 A EP 0731696 A JP 9506368 T US 5714484 A US 5663380 A US 5925772 A	23-01-1996 27-06-1995 15-06-1995 18-09-1996 24-06-1997 03-02-1998 02-09-1997 20-07-1999
WO 9640647 A	19-12-1996	US 5714484 A AU 713934 B AU 6100996 A CA 2223268 A EP 0863883 A JP 11507912 T	03-02-1998 16-12-1999 30-12-1996 19-12-1996 16-09-1998 13-07-1999

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/26278

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5691368 A	25-11-1997	AU 692044 B	28-05-1998
		AU 4473196 A	31-07-1996
		CA 2210258 A	18-07-1996
		CN 1173174 A	11-02-1998
		EP 0802909 A	29-10-1997
		FI 972935 A	10-07-1997
		HU 77649 A	28-07-1998
		JP 10512257 T	24-11-1998
		NO 973216 A	09-09-1997
		NZ 298999 A	28-01-1999
		WO 9621655 A	18-07-1996
		ZA 9600100 A	24-07-1996
WO 9924460 A	20-05-1999	AU 1487399 A	31-05-1999

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